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Small Intestinal Bacterial Overgrowth

A clinician's guide to evaluation and treatment

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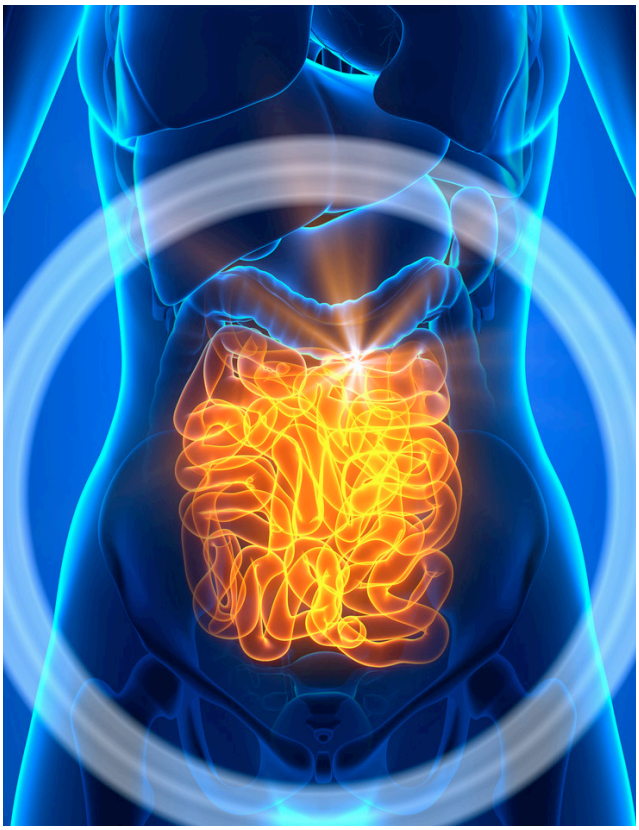
Overview

Small intestinal bacterial overgrowth (SIBO) is characterized by an increase in the number or a change in the type of bacteria growing in the small intestine. SIBO can be marked by overgrowth of pathogenic bacteria or beneficial bacteria, but any overgrowth becomes detrimental to gastrointestinal and systemic health.

SIBO has been a subject of interest in the international gastroenterology community since the late 1990s, and awareness of the condition has spread rapidly over the last decade. Despite general medical consensus on the foundational causes, manifestations, and treatments for SIBO, many aspects of this condition remain a mystery.

Current research is exploring relationships between SIBO and irritable bowel syndrome (IBS), mood disorders, autoimmune diseases, skin diseases, impaired methylation, and genomics. As researchers discover more about the complex interactions between the intestinal microbiome and other body systems, dysbiotic conditions like SIBO become increasingly relevant.

In this guide for clinicians, we review the current research related to the causes, symptoms, diagnosis, and treatment of SIBO.



Risk Factors for SIBO

The causes of SIBO are varied and still under active investigation. We do know that SIBO develops when 1 or more defense mechanisms against bacterial overgrowth become compromised. These defense mechanisms include hydrochloric acid to destroy bacteria in the stomach; gut motility to keep intestinal contents moving forward; immunoglobulins and pancreatic proteolytic enzymes to halt bacterial growth; and an intact ileocecal valve to prevent backflow of contents from the large intestine to the small intestine.

Risk factors for SIBO include achlorhydria, chronic use of acid-blocking medications, chronic pancreatitis, diabetic neuropathy, and immunodeficiency. Impairment of the migrating motor complex (MMC), which creates waves of smooth muscle contraction to cleanse the gastrointestinal tract, is another important risk factor. Mark Pimentel, MD, a researcher in the division of gastroenterology at Cedars-Sinai Medical Center, has also proposed that acute gastroenteritis (ie, food poisoning) may lead to changes in gut innervation, subsequent motility problems, and the manifestation of SIBO.

SIBO is more prevalent in patients with other gastrointestinal disorders, including celiac disease, Crohn's disease, and irritable bowel syndrome (IBS), than it is in the general population. A 2014 review by Ghoshal, et al reported that the frequency of SIBO in patients with IBS ranges from 4% to 78%, and Dr. Pimentel and his colleagues at Cedars-Sinai Medical Center detected evidence of SIBO in 84% of patients with IBS.

It is thought that the disruption in gut motility and immune function accompanying chronic digestive disorders predisposes to the development of SIBO. In some cases, however, it is difficult to determine whether SIBO precedes or results from other digestive disorders. This is particularly true for the complex relationship between SIBO and IBS.

Signs and Symptoms of SIBO

SIBO often (but not always) involves nonspecific digestive symptoms. These symptoms result from bacterial fermentation of short-chain carbohydrates. Chronic diarrhea, constipation, abdominal distention, cramping, nausea, acid reflux, flatulence, and belching are common. The digestive symptoms of SIBO are often indistinguishable from the digestive symptoms of IBS or other functional digestive disorders.

As SIBO progresses, signs of malabsorption may predominate, such as steatorrhea, weight loss, malnutrition, or osteoporosis. Systemic symptoms can also result because of disruption in intestinal barrier function: joint pains, skin rashes, mood changes, fatigue, or autoimmune diseases can co-occur.

In some cases, abnormal laboratory results are the first clue of the presence of SIBO. Iron-deficient anemia, marked by low ferritin levels, can result from a combination of occult blood loss and bacterial uptake of iron in the intestines. Vitamin B12 deficiency can also result from bacterial uptake, producing macrocytic anemia. Malabsorption contributes to deficiencies of fat-soluble vitamins, including vitamins A, E, and D. In contrast, levels of vitamin K and folate may increase as a result of bacterial synthesis.

Clinical Clues that Suggest Possible SIBO

If a patient has an idiosyncratic response to a reasonable intervention, this may be the first clue that SIBO exists. Following are some clinical clues that suggest possible underlying SIBO:

- Transient improvement of chronic digestive problems after antibiotics
- Worsening of chronic digestive problems from prebiotics or probiotics (because prebiotics fuel bacterial growth)
- Worsening of constipation from a high-fiber diet (because fiber fuels bacterial growth)
- Insufficient improvement from a gluten-free diet in patients with celiac disease
- Chronic digestive symptoms after taking opioid medications (because opioids compromise gut motility)

Diagnosis of SIBO

The diagnosis of SIBO has been met with some resistance in the conventional medical community because of the lack of standardized guidelines defining its diagnosis. This resistance may soon shift, thanks to work recently conducted by the North American Consensus group on hydrogen and methane-based breath testing. In a paper published in the spring of 2017, the North American Consensus group agreed on 26 statements related to the indications, preparation, protocols, and interpretation of breath tests. Importantly, the group had 100% agreement that hydrogen/methane breath testing is indicated for the diagnosis of SIBO.

Hydrogen/Methane Breath Testing

Breath testing relies on the concept that ingested sugars will be fermented by bacteria in the small intestine, creating gases (hydrogen and methane) that diffuse into the bloodstream and are released in expired air. Hydrogen and methane are exclusively produced in the large intestine in healthy humans but also produced in the small intestine in patients with SIBO.

The clinician can choose to use glucose or lactulose as the substrate for the hydrogen/methane breath test. Glucose is available to patients without a prescription, whereas lactulose is only available with a prescription. Each offers different advantages. Statistics on the sensitivity and specificity of each test vary greatly, but one advantage of lactulose is that it is more likely to detect SIBO in the most distal portion of the small intestine. This is because glucose is absorbed in the proximal small bowel, and lactulose passes all the way to the colon.

The North American Consensus group established guidelines for preparation (table 1) and performance of hydrogen/methane breath tests. They suggest up to a maximum dose of 75g of glucose with 1 cup (8 ounces) of water and the correct dose of lactulose is 10g with 1 cup (8 ounces) of water. The patient collects a baseline sample of expired air and then consumes either glucose or lactulose in water. The patient then collects samples of expired air every 20 minutes for 3 hours.

Table 1. Patient Preparation for Hydrogen/Methane Breath Test*

- Antibiotics should be avoided 4 weeks before the breath test (this pertains only to the initial test; follow-up testing can be done immediately after antibiotics to assess response to treatment)
- Prokinetic drugs and laxatives should be stopped 1 week before breath testing
- Fermentable foods, such as complex carbohydrates, should be avoided on the day before breath testing
- The patient should fast 8-12 hours before breath testing

* Stated by the North American Breath Testing Consensus

Culture of jejunal aspirate has historically been considered the benchmark test for SIBO diagnosis, with the presence of more than 10^4 or 10^5 colony-forming units (CFUs) of bacteria per milliliter indicating a positive diagnosis. However, the recent North American Consensus statement concludes that small bowel culture is not satisfactory for the assessment of SIBO and, if it is used, a cutoff of more than 10^3 CFUs/ml should define SIBO. One challenge with relying on small bowel aspiration to diagnose SIBO is that the collection of fluid is localized to the proximal portion of the small bowel, yet many cases of SIBO occur in the distal portion. Small bowel aspiration requires endoscopy, which is invasive, time-consuming, and costly.

The North American Consensus Group had 100% agreement that hydrogen/methane breath testing is indicated for the diagnosis of SIBO.

Hydrogen/Methane Breath Test Interpretation

Certain bacteria, including *Enterobacteriaceae*, *Bacterioides*, and *Clostridium*, produce primarily hydrogen rather than methane. Other bacteria, collectively called methanogens, produce primarily methane. These are members of the domain *Archaea*, including *Methanobrevibacter* and *Methanospaere* species. The North American Consensus group recommends that hydrogen, methane, and carbon dioxide all be measured simultaneously during breath testing.

The consensus group was the first to establish guidelines for the interpretation of hydrogen/methane breath tests. They state the following:

- A rise of ≥20 ppm from baseline in hydrogen by 90 minutes should be considered positive for SIBO
- Two peaks on breath test are not required for the diagnosis of SIBO
- The level of ≥10 ppm for methane should be considered positive for SIBO

False positive results of the hydrogen/methane breath test are extremely rare and most likely a result of faulty test preparation. If a test result is positive, the clinician and patient can feel confident that SIBO does indeed exist.

Treatment of SIBO

SIBO is a chronic and relapsing condition in the majority of cases. Lauritano et al reported in 2008 that 44% of patients treated successfully with antibiotics relapse within 9 months. Treatment involves cyclical antimicrobial therapy, prokinetic agents, nutrient supplementation, dietary interventions, and treatment of comorbid conditions. The interventions discussed here are antibiotics, herbal antimicrobials, probiotics, prokinetics, and diet.

Antibiotics

Rifaximin is the most widely studied antibiotic for SIBO. It is a broad-spectrum antibiotic that is effective against gram-positive and gram-negative bacteria and against aerobes and anaerobes. Rifaximin is unique in that it is not systemically absorbed but rather acts selectively within the small intestine. Despite its antibiotic effect, it also has a eubiotic effect, promoting growth of beneficial *Bifidobacteria* and *Lactobacilli*, and it does not predispose to overgrowth of yeast or *Clostridium difficile*. Studies show that rifaximin at dosages of 1,200 to 1,600 mg per day for 10-14 days is effective at eradicating SIBO in the majority of patients.

Rifaximin is most effective for diarrhea-predominant SIBO (or when hydrogen production dominates). For cases of constipation-predominant SIBO (or when methane production dominates), the combination of rifaximin with neomycin has greater efficacy. Metronidazole and other antibiotics are also occasionally used.

Herbal Antimicrobials

Herbal antimicrobials are a consideration for patients who do not respond to antibiotics, who relapse frequently, or who simply have a personal preference to opt for natural therapies. There is one additional reason to consider herbal antimicrobials: small intestinal

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fungal overgrowth (SIFO). In a 2013 study published by Jacobs, et al, researchers found that SIBO and SIFO coexisted in 34% of patients with unexplained gastrointestinal symptoms. If patients with SIBO are treated with antibiotics, there is a risk of exacerbating undiagnosed SIFO. Many antimicrobial herbs have both antibacterial and antifungal properties, mitigating this risk.

A study published by Chedid, et al in 2014 reported that herbal therapy is as effective as rifaximin in the treatment of SIBO. The herbal combinations used for the study were proprietary blends that provided more than a dozen different herbs, including red thyme oil, oregano oil, berberine sulfate, ginger, and numerous traditional Chinese herbs. Despite the complexity of the protocol tested, this study provided evidence in favor of using herbal interventions for SIBO.

Aside from the Chedid study, there is scant research on the efficacy of herbal interventions for the eradication of SIBO. Most evidence is anecdotal or based on mechanistic and animal studies. Despite the paucity of research in this area, there are several herbs that are used clinically for their antimicrobial effects.

Antimicrobial herbs with anecdotal evidence to treat all types of SIBO:

- Berberine
- Oregon Grape (*Mahonia aquifolium*) or other berberine-containing herbs
- Mugwort (*Artemesia vulgaris*)
- Pomegranate (*Punica granatum*)
- Oregano (*Origanum vulgare*)
- Neem (*Azadirachta indica*)
- Enteric-Coated Peppermint Oil (*Mentha piperita*)
- Clove (*Syzygium aromaticum*)

Antimicrobial herbs with anecdotal evidence to treat methane-predominant SIBO:

- Allicin, an organosulfur compound obtained from garlic
- Quebracho tannins

Probiotics

Probiotic and prebiotic supplementation in patients with SIBO is complicated. SIBO is characterized by excessive growth of any bacteria—even beneficial bacteria. Probiotic supplementation has the potential to increase the bacterial load. Prebiotics, including fructo-oligosaccharides and inulin, can be even more detrimental. Prebiotics provide fuel for bacterial growth and are routinely reported by clinicians to exacerbate SIBO.

Despite the potential for probiotics to exacerbate SIBO, a few small clinical trials suggest that probiotics may actually be helpful in eradicating SIBO. Probiotic strains that have shown promise include *Lactobacillus casei* and *Lactobacillus acidophilus*. In addition, a pilot study published by Rosania, et al in 2013 reported that cyclical treatment with *L. casei* between rounds of antibiotics was an effective strategy to eradicate SIBO, and another published by Khalighi, et al in 2014 reported that *Bacillus coagulans* spores reduced complications during maintenance care.

Until further research clarifies the interaction between probiotics and SIBO, the most prudent use of probiotic supplementation appears to be either between rounds of antibiotics or during maintenance care.

Prokinetic Agents

Given that impairment of the MMC underlies many cases of SIBO, prokinetic agents are prescribed to stimulate gastrointestinal motility. These are often prescribed cyclically, between courses of antibiotics or antimicrobial therapies. They are most effective if dosed

SYZYGIUM AROMATICUM

at bedtime to stimulate motility during the fasting state overnight. Prescription prokinetic agents include low-dose erythromycin, low-dose prucalopride, and low-dose naltrexone.

Natural prokinetic agents include ginger, herbal bitters (eg, gentian root, dandelion root and leaf, burdock root), and a formulation called Iberogast. Iberogast is an herbal product that includes chelidonium leaf (*Chelidonium*), milk thistle fruit (*Cardui mariae*), lemon balm leaf (*Melissa officinalis*), carum (*Carvi fructus*), licorice root (*Glycyrrhiza*), angelica root (*Angelica*), chamomile flower (*Matricaria*), and peppermint leaf (*Mentha piperita*). A 2002 systematic review reported Iberogast to be equally as effective as prescription prokinetic agents for relieving functional gastrointestinal symptoms.

Diet

Dietary changes are imperative for successful treatment and maintenance of SIBO. Intestinal bacteria feed on carbohydrates—including starches, soluble fiber, and fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs). For this reason, any diet recommended for patients with SIBO should be low in carbohydrates.

One therapeutic option for patients with SIBO is the elemental diet. The elemental diet is a medical food that provides all of the macronutrients and micronutrients required for survival. Protein is in the form of amino acids, fat is in the form of medium chain and other triglycerides, and carbohydrates are in the form of glucose or glucose polymers. The nutrients in the elemental diet are predigested so they leave no residue. To be effective, the elemental diet must be followed for 2 to 3 weeks, during which time no additional food can be eaten. Dr. Pimentel and his colleagues reported in a 2004 study that 2-weeks of the elemental diet normalized the lactulose breath test and significantly improved symptoms in patients with SIBO.

Other dietary recommendations for patients with SIBO often combine features from the Specific Carbohydrate Diet (SCD), the Gut and Psychology Syndrome (GAPS) diet, the low FODMAP diet, and the Bi-Phasic Diet. These 4 diets all restrict certain carbohydrate foods, but none of the diets are specific to SIBO (table 2). These diets can be customized for each patient, depending on food sensitivities and allergies. They can be implemented during treatment, during maintenance, or for the prevention of SIBO.

In addition to the types of foods eaten, the timing of meals can also influence symptoms of SIBO. This is because of the action of the MMC. The MMC produces waves of contraction through the gastrointestinal tract during periods of fasting. These waves have a mechanical cleansing effect on the empty stomach and intestines, sweeping contents forward. To allow for the MMC to cycle effectively, meals must be spaced at 4-5 hours, and the overnight fast should ideally be 12 hours.

Table 2. Comparison of the SCD, GAPS Diet, Low-FODMAP Diet, and the Bi-Phasic Diet for SIBO

Diet	Primary Recommendations		Cautions in SIBO
SCD	Include the following: • Meat, fish, poultry • Eggs • Some beans • Lactose-free dairy • Non-starchy vegetables • Ripe fruit • Nuts and seeds • Honey	Eliminate the following: • Grains • Starchy vegetables • Lactose • Any sweeteners besides honey and occasional stevia	Beans are a source of fermentable carbohydrates that can exacerbate SIBO Heavy reliance on fruits and honey can provide fermentable substrates for bacterial growth
GAPS Diet	Similar to SCD with these exceptions: • Fewer beans • Incorporates principles of the Weston A. Price Foundation • Emphasizes bone broths and lacto-fermented foods		Fermented foods might increase the bacterial load and exacerbate symptoms of SIBO
Low-FODMAP Diet	Allow low-FODMAP foods, including: • Lactose-free dairy, rice milk, coconut milk, almond milk • Cane sugar, maple syrup • Berries, grapes, melon, bananas, citrus • Most vegetables except those listed at right • Oats, rice, quinoa • Tofu • Nuts and seeds except those listed at right	Eliminate high-FODMAP foods, including: • Milk, yogurt, ice cream • Honey, agave • Dried fruit, juice • Apples, pears, stone fruits, watermelon • Garlic, onions, cruciferous vegetables, mushrooms, corn • Wheat, barley, rye • Beans • Pistachios, cashews	The low-FODMAP diet does not eliminate polysaccharide-rich foods, such as grains and starchy vegetables, which can exacerbate SIBO
Bi-Phasic Diet by Nirala Jacobi, BSc, ND	Phase 1 (4-6 weeks): • Repair intestinal lining • Eliminate all grains, legumes, dairy, sugar, certain vegetables, and fermented foods	Phase 2 (4-6 weeks): • Remove bacteria with antimicrobials • Diet becomes more lenient and similar to the low-FODMAP or SCD	Prebiotics are suggested during phase 2, but this might exacerbate bacterial overgrowth

Conclusion

SIBO is characterized by excessive growth of bacteria in the small intestine, but its many causes, manifestations, and comorbid conditions make it much more complex than a simple infection.

SIBO should be considered in any patient with functional digestive symptoms. It should also be considered in patients who develop autoimmune disease, skin disease, mood disorders, or osteoporosis with no evident cause or who progress despite reasonable care. Clinical clues for SIBO include aggravation from prebiotics or fermented foods, transient improvement in gastrointestinal symptoms after a course of antibiotics, and onset of chronic digestive symptoms after food poisoning. SIBO may be one of the most under-diagnosed conditions underlying a wide range of chronic diseases.

The hydrogen/methane breath test is the simplest and most cost-effective way to identify SIBO and to monitor the response to care. With targeted antimicrobial therapies, prokinetic agents, dietary changes, and other therapies to support gastrointestinal function, patients with SIBO can overcome symptoms and experience revitalized health.

Selected References

Bures J, Cyrany J, Kohoutova D, et al. Small intestinal bacterial overgrowth syndrome. *World J Gastroenterol*. 2010;16(24):2978-2990.

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.

Dukowicz AC, Lacy BE, Levine GM. Small intestinal bacterial overgrowth: a comprehensive review. *Gastroenterol Hepatol (N Y)*. 2007;3(2):112-122.

Gabrielli M, D'Angelo G, Di Rienzo T, Scarpellini E, Ojetti V. Diagnosis of small intestinal bacterial overgrowth in the clinical practice. *Eur Rev Med Pharmacol Sci*. 2013;17 Suppl 230-35.

Gasbarrini A, Corazza GR, Gasbarrini G, et al. Methodology and indications of H2-breath testing in gastrointestinal diseases: the Rome Consensus Conference. *Aliment Pharmacol Ther*. 2009;29 Suppl 11-49.

Ghoshal UC, Ghoshal U, Das K, Misra A. Utility of hydrogen breath tests in diagnosis of small intestinal bacterial overgrowth in malabsorption syndrome and its relationship with oro-cecal transit time. *Indian J Gastroenterol*. 2006;25(1):6-10.

Ghoshal UC. How to interpret hydrogen breath tests. *J Neurogastroenterol Motil*. 2011;17(3):312-317.

Ghoshal UC, Srivastava D. Irritable bowel syndrome and small intestinal bacterial overgrowth: meaningful association or unnecessary hype. *World J Gastroenterol*. 2014;20(10):2482-2491.

Jacobs C, Coss Adame E, Attaluri A, Valestin J, Rao SS. Dysmotility and proton pump inhibitor use are independent risk factors for small intestinal bacterial and/or fungal overgrowth. *Aliment Pharmacol Ther*. 2013;37(11):1103-1111.

Khalighi AR, Khalighi MR, Behdani R, et al. Evaluating the efficacy of probiotic on treatment in patients with small intestinal bacterial overgrowth (SIBO)–A pilot study. *Indian J Med Res*. 2014;140(5):604-608.

Lauritano EC, Gabrielli M, Scarpellini E, et al. Small intestinal bacterial overgrowth recurrence after antibiotic therapy. *Am J Gastroenterol*. 2008;103(8):2031-2035.

Logan AC, Beaulne TM. The treatment of small intestinal bacterial overgrowth with enteric-coated peppermint oil: a case report. *Altern Med Rev*. 2002;7(5):410-417.

Peralta S, Cottone C, Doveri T, Almasio PL, Craxi A. Small intestine bacterial overgrowth and irritable bowel syndrome-related symptoms: experience with Rifaximin. *World J Gastroenterol*. 2009;15(21):2628-2631.

Pimentel M, Chow EJ, Lin HC. Normalization of lactulose breath testing correlates with symptom improvement in irritable bowel syndrome, a double-blind, randomized, placebo-controlled study. *Am J Gastroenterol*. 2003;98(2):412-419.

Pimentel M, Constantino T, Kong Y, Bajwa M, Rezaei A, Park S. A 14-day elemental diet is highly effective in normalizing the lactulose breath test. *Dig Dis Sci*. 2004;49(1):73-77.

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.

Rosania R, Giorgio F, Principi M, et al. Effect of probiotic or prebiotic supplementation on antibiotic therapy in the small intestinal bacterial overgrowth: a comparative evaluation. *Curr Clin Pharmacol*. 2013;8(2):169-172.

Saller R, Pfister-Hotz G, Iten F, Melzer J, Reichling J. [Iberogast: a modern phytotherapeutic combined herbal drug for the treatment of functional disorders of the gastrointestinal tract (dyspepsia, irritable bowel syndrome)—from phytomedicine to "evidence based phytotherapy." A systematic review]. *Forsch Komplementarmed Klass Naturheilkd*. 2002;9 Suppl 11-20.

Saad RJ, Chey WD. Breath testing for small intestinal bacterial overgrowth: maximizing test accuracy. *Clin Gastroenterol Hepatol*. 2014;121964-72.

Shah SC, Day LW, Somsouk M, Sewell JL. Meta-analysis: antibiotic therapy for small intestinal bacterial overgrowth. *Aliment Pharmacol Ther*. 2013;38(8):925-934.

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