Small intestinal bacterial overgrowth (SIBO) is characterized by an overgrowth of various types of bacteria in the small intestine, bacteria which are largely only found in the colon. SIBO was initially thought of as a rare condition; however, it is now recognized as a more prevalent digestive disorder than previously acknowledged. A meta-analysis has shown the prevalence of SIBO to be approximately 64% among patients with irritable bowel syndrome (IBS).[1] The symptoms of SIBO vary, from mild (constipation, gas, bloating) to suffering from chronic diarrhea, weight loss, and malabsorption. It has been realized that the symptoms of SIBO closely overlap symptoms of IBS, which allows for most patients to be wrongly diagnosed with IBS.

**Definition**

SIBO is defined as a bacterial population in the small intestine that exceeds $10^5$ to $10^6$ organisms per millilitre and contains certain types of organisms, specifically coliform bacteria.[2] The large intestine contains an average count of $10^{14}$ bacteria per millilitre, which is where the majority of the gut microbiota resides. To compare, the small intestine normally contains less than $10^5$ bacteria per millilitre, and most of these are Gram-positive aerobic bacteria (Figure 1). This low amount of bacteria in the small intestine is due to sufficient gastric acid secretion, normal peristalsis, normal secretory IgA levels, and an intact ileocecal valve.[4]

**Etiology and Pathophysiology**

SIBO occurs most commonly when there is abnormal gastric acid secretion and/or intestinal clearance, which result in deviant bacterial migration in the GI tract. Some
conditions that predispose patients towards the development of SIBO include achlorhydria (from autoimmune or iatrogenic causes or surgery), diverticulosis, systemic diseases (e.g. celiac disease, Crohn’s disease), intestinal obstruction, immune deficiency states (including secretory IgA deficiency), and alcoholism.[1] The elderly population is more susceptible, as gastric acid production decreases with age. Once the bacterial overgrowth has been established, an inflammatory response to this dysbiosis occurs in the intestinal mucosa, caused by the bacteria’s toxic by-products. Analysis of small-intestine biopsies in the elderly diagnosed with SIBO has shown blunting of the intestinal villi, thinning of the mucosa, and increased white blood cells.[2]

Symptoms and Signs Explained
Symptoms associated with bacterial overgrowth include bloating, abdominal pain or discomfort, diarrhea, constipation, fatigue, weakness, and abdominal distension. The severity of symptoms reflects the amount of overgrowth as well as the extent of inflammation in the small intestine.[2] The symptoms of SIBO can be nonspecific, which can make it difficult to differentiate from conditions such as IBS, lactose or fructose intolerance, celiac disease, or Crohn’s disease.

In patients with SIBO, carbohydrates ingested will be fermented by the excess bacteria in the small intestine, which leads to increased gas production resulting in bloating and flatulence.[5] The gases produced include hydrogen and methane. Evidence suggests that excessive methane is produced by this overgrowth, and the presence of methane results in constipation.[6] Studies show that a reduction in breath methane by modification of the gut flora improves this constipation.[6] On the other hand, the thinning of the mucosa caused by the bacterial overgrowth has been shown to increase the osmotic load, resulting in diarrhea. Studies have demonstrated that IBS patients with confirmed SIBO more often have diarrhea-predominant IBS.[6]

Complications of SIBO
The symptoms of SIBO can reflect the complications of the condition, including motility issues, malabsorption, and nutritional deficiencies. The complications of SIBO vary from mild digestive discomfort to severe malabsorption issues, leading to multiple nutrient deficiencies, especially fat-soluble vitamin deficiencies. Deficiencies in fat-soluble vitamins occur from poor absorption as a result of bacterial deconjugation of bile salts.
Symptoms of severe deficiency can include night blindness (vitamin A), osteomalacia (vitamin D), prolonged prothrombin times (vitamin K), and immune impairments from altered T-cell functioning.\[2\]

Vitamin B$_{12}$ deficiency is a common complication of SIBO. Studies with human subjects with atrophic gastritis and bacterial overgrowth absorbed less vitamin B$_{12}$ compared to controls. This deficiency was reversed with antibiotic therapy, indicating the importance of modifying gut flora as a treatment.\[2\]

Carbohydrate and protein malabsorption commonly occur as well, due to the premature fermentation and breakdown by the excess bacteria in the small intestine.

**Diagnosis**

Diagnosis of SIBO is difficult and controversial, due to the low specificity of the symptoms and absence of definitive objective diagnostic tests. Two tests are used to diagnose SIBO: bacterial culture and the more predominant method, breath tests.\[2\] The most direct method of assessing the bacteria in the gut is the quantitative measurement of bacteria counts via culture. However, this method requires an invasive and costly endoscopic procedure and commonly encountered problems include contamination, difficulty aspirating a sufficient sample, and introduction of air into the lumen of the duodenum.\[2\]

The challenges of this method led to the development of indirect methods of measuring small-bowel bacteria and diagnosing SIBO. Breath-testing is now the most common method to assess patients for SIBO. The breath tests used all rely on the measurement of exhaled gases produced by the bacteria's metabolism of an ingested substrate (usually a simple carbohydrate such as lactulose, glucose, sucrose, or xylose). Patients are generally instructed to avoid eating unfermentable complex carbohydrates and to fast overnight. After an overnight fast, a hydrogen and/or methane sample is taken, and then the patient consumes 10 g of lactulose or 50–80 g of glucose administered in a small glass of water. Breath samples are then collected every 15–30 minutes for a total of 3–4 hours.\[2\]

There are a few complications with the SIBO breath test, including a lack of consensus regarding what the gold standard is for diagnosing SIBO, as well as fairly high rates of false negatives.\[2\]
Treatment

The therapeutic approach to SIBO involves addressing the predisposing condition and is supported by antibiotics (herbal and/or conventional), probiotics, and diet modification. The goal of therapy is to restore normal small intestinal flora and additionally, to correct any nutritional deficiencies.

“An ounce of prevention is worth a pound of cure.”
—Benjamin Franklin

Protective factors that prevent the development of SIBO include adequate gastric acid production and secretion, pancreatic enzymes, proper motility and elimination, biofilm, sufficient secretory IgA, and bile acids.[1]

Once the diagnosis for SIBO has been confirmed, the standard treatment involves a course of the antibiotic rifaximin (1200 mg a day for 10–14 days). Rifaximin is the most commonly studied treatment for SIBO, and has shown a breath-test resolution rate of 49.5% in eight clinical trials. However, a meta-analysis showed that the therapeutic efficacy of this antibiotic in the long term was only 9.8%.[1] Antibiotics are also well-known to have a wide range of toxicity, adverse effects, and resistance; also, recurrence rates after rifaximin treatment has been shown to be high.[1] A clinical trial showed the combination of rifaximin with partially hydrolysed guar gum seems to reduce the recurrence rates of SIBO compared to rifaximin alone.[7]

A study compared the efficacy of herbal therapy to antibiotic therapy in the setting of SIBO.[1] The study’s response rate for normalizing breath hydrogen testing in patients with SIBO was 46% for herbal therapies v. 34% for rifaximin. In this study, a combination of antimicrobial herbs was used including berberine extracts, oil of oregano, wormwood, and Thymus vulgaris. The researchers concluded that patients receiving antibiotic or herbal therapy received a similar response rate and safety profile. They also found that in patients refractory to rifaximin, herbal therapy serves as a potential therapy with equivalent efficacy to triple antibiotics.[1]
Some studies support the use of probiotics as an effective treatment for IBS; however, attempts at treating SIBO with probiotics have shown mixed results. One study using *Lactobacillus* showed an improvement in symptoms and a reduction in hydrogen breath levels; however, other studies have not shown improvements.[2]

A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) was shown to reduce the symptoms of IBS and have marked effects on gut microbiota. The long-term effects of a low intake of FODMAPs require further study.[8]

**Conclusion**

The human body contains at least ten times more microbial cells than human cells, with most of these cells concentrated in the gastrointestinal tract.[3] There is more recent interest in the microbiome, more specifically the gut flora and its relation to intestinal function and the development of various diseases. Given the role of the gut microbiome in disease, SIBO is an important gastroenterological condition to identify and treat. Studies thus far reveal encouraging results on modifying the gut flora as a therapeutic modality for SIBO, and further investigations are necessary to reveal the optimal and most successful diagnostic and treatment tools.

**References**