KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Identifying Gut Pathologies: Small Intestinal Bacterial Overgrowth Breath Test (Part 1)

Welcome, everybody, to the gut [small intestinal bacterial overgrowth] (SIBO) Functional Medicine track. We're going to talk about SIBO, [and there are] lots of definitions that continue to be debated. But the principal concept is that normal small bowels should have lower levels of microbial colonization compared with the colon, and this is normal balance. It's significantly altered in SIBO. So, in the simplest definition, SIBO is defined as the presence of excessive numbers of bacteria in the small bowel causing gastrointestinal symptoms.

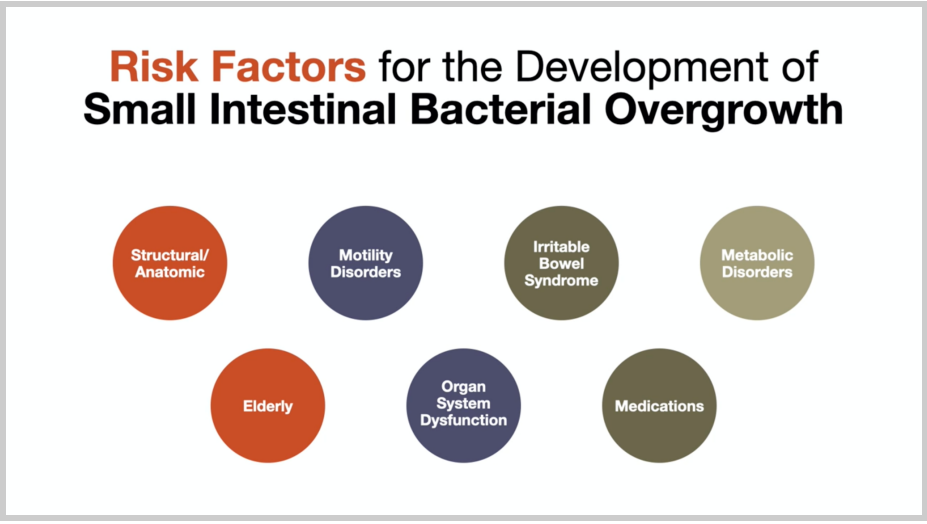
The most recent North American Consensus found that the literature points more accurately to the definition of SIBO as a bacterial colony count of greater than or equal to 10 to the third [power] colony formation units per milliliter, or CFU per milliliter, in a duodenal or jejunal aspirate as being indicative of SIBO. This is based on a collation of the literature among normal subjects in different trials. It should also be noted that the bacterial colony counts in SIBO are based on growth of actual cultural bacteria.

In addition to the absolute number of bacteria in the small intestine, the type of flora also plays a role in the signs and symptoms of SIBO. The predominant bacteria metabolize bile salts to unconjugated or insoluble compounds, and that can cause fat malabsorption or bile acid diarrhea. And microorganisms that preferentially metabolize carbohydrates to short-chain fatty acids in gas can cause bloating without diarrhea, whereas gram-negative bacteria that are overgrown in the small intestine, like *Klebsiella*, can produce toxins that damage the mucosa and interfere with nutrient absorption. This explain[s] why people with SIBO can have such a wide variety and range of symptoms. It really depend[s] on which type of bacteria is overgrown in the small intestine.

Prevalence of SIBO is difficult to determine given the lack of consensus on how to define it and the fact that there's no gold standard test or even an accepted interpretation of those tests. There [are] also no studies about evaluating SIBO in healthy volunteers. The data that we have on healthy volunteers with SIBO come from the control group of trials. And if you look at these

control groups, you see a prevalence of SIBO in healthy people that can range from 6 to 20 percent depending on what test method is used, whether they're using endoscopy to define SIBO or [a] glucose breath test or lactulose breath test. And I always wonder what "healthy people" actually mean[s] in these control groups and studies. But if we take it at face value and we say that the control group in these studies had no digestive symptoms and no significant diseases, then you could maybe guess that 6 to 20 percent of them have SIBO in these studies. The rates of SIBO in asymptomatic young or even middle-aged people seem to be on the lower end of the scale, whereas the rates of SIBO in asymptomatic elderly patients tend to be on the higher end of that scale. And again, the definition of healthy here, I think, makes a difference. Also, the understanding of what symptoms could be related to SIBO makes a difference. So if you have a healthy cohort in one of these studies who has no gut symptoms as the [American College of Gastroenterology's] SIBO definition describes, but they do have skin problems or brain fog or things like that, [which] may not be the typical symptoms that are associated with SIBO, they're still labeled as a healthy control and labeled as a healthy person [who] maybe also happens to have SIBO rather than a person with SIBO [who's] experiencing a direct result of that pathology. So these numbers are a little bit misleading. But the key takeaway is that some patients can have what is defined as SIBO and not necessarily be symptomatic. I've certainly seen this in my practice, and we'll talk a little bit more about this as we go into various relevant sections.

The pathogenesis of SIBO and how it develops is not entirely clear, and it's still somewhat controversial. But I think we're getting closer to having a general consensus of risk factors. The basic idea is that it develops when the normal homeostatic mechanisms that control small intestinal bacterial populations are disrupted. And at least seven risk factors have been identified as potential predisposing triggers for that disruption.



One would be structural or anatomic issues. And this can be present, for example, after surgery or if there was damage to nerves that innervate the small intestine or [in] patients with cystic fibrosis or other conditions that cause structural or anatomic abnormalities. We have motility disorders, like [diabetes], or dysfunction of the migrating motor complex, which we'll [talk] about later. We've got conditions like irritable bowel syndrome, which is really a non-specific condition, a diagnosis of exclusion, as we call it. And my guess is that that's more related to the disrupted gut microbiome that becomes a predisposing factor for SIBO. Then [there are] metabolic disorders like diabetes and low stomach acid, elderly age, as we just talked about, or even organ system dysfunction, and medications.

In a Functional Medicine practice, there are three primary processes that contribute to SIBO. Number one [is] gastric acid secretion, so low stomach acid in particular. Number two [is] small intestine dysmotility. So this again involves disruption of the migrating motor complex and that peristaltic wave in the gut, which has this cleansing action and prevents the overgrowth of bacteria, and then also a disrupted gut microbiome. And by this, I'm more referring to dysbiosis in the colon that then leads to overgrowth of bacteria in the small intestine. Once it's present, SIBO has been shown to cause inflammation in the small intestine, blunting of the small intestinal villi, which are responsible for the digestion and absorption of food, thinning of the small intestine mucosa, and crypts. It can also further reduce stomach acid production and further slow motility, which then causes this vicious cycle and exacerbates SIBO. So low stomach acid and slow motility can cause SIBO. But then SIBO can cause low stomach acid and slow motility, which makes it much more likely that SIBO will recur or be recalcitrant and difficult to get rid of.

Let's take a look more closely at each of these key processes. Stomach acid suppresses the growth of ingested bacteria, which would limit bacterial counts in the upper small intestine. And

that's why hypochlorhydria, or low stomach acid, is a primary risk factor for SIBO. It can develop when [*Helicobacter*] *pylori* is present or with chronic stress or as a consequence of aging. SIBO can lead to a false positive for *H. pylori*, in fact, using breath testing given the presence of urease-positive bacterial strains in the upper part of the small intestine. You may know that breath testing for *H. pylori* measures levels of urea in the breath. What I just said was that in SIBO, you can have an overgrowth of certain types of bacteria in the upper part of the small intestine that also produce urea. And that can lead to a false positive for *H. pylori* in the breath test. That's one of the reasons I prefer fecal antigen testing for *H. pylori* as the first-line testing. There are also drugs that inhibit acid secretion, like histamine 2 receptor blockers or [proton pump inhibitors], both of which are used to treat heartburn and [gastroesophageal reflux disease]. So if a patient has heartburn, they [take] these acid-suppressing drugs for a significant period of time. It reduces the stomach acid, in some cases, almost to zero and then predisposes them to [develop] SIBO. It's another reason why I'm really uncomfortable with patients using these drugs for a long period of time. They were never designed or even approved to be used for that length of time.

The next primary trigger is impaired intestinal motility or motility disorders in general. During periods of fasting, the migrating motor complex, or the MMC, develops approximately every 90 to 120 minutes. And what it does is it sweeps residual debris through the gastrointestinal tract. So abnormalities in the migrating motor complex may predispose to the development of SIBO. We'll dive into this a little bit more throughout the presentation when we talk about the IBS-smart test and ways to assess for immune-mediated causes of an impaired migrating motor complex. Also, gastroparesis, which is a chronic problem of delayed gastric emptying or the emptying of the stomach contents into the small intestine, can develop as a secondary complication of diabetes. This explains the connection between diabetes and metabolic disorders and SIBO. And then there are also neurological and myopathic disorders, such as intestinal pseudo-obstruction and scleroderma or polymyositis, respectively. These are all associated with SIBO development, as well. The third factor is [a] disrupted gut microbiome. There's a little less research on this proving a direct correlation or connection. But there are several lines of evidence, I believe, to support an association.

One is that it's well-established that antibiotic use can lead to [a] disrupted gut microbiome, and in turn, SIBO. Celiac disease leads to a disrupted gut microbiome, and there's a strong connection between celiac [disease] and SIBO. [A] disrupted gut microbiome has been shown to cause dysfunction of the ileocecal valve. And we know that dysfunction of the ileocecal valve can lead to translocation of bacteria that should stay in the large intestine up into the small intestine, which is one of the main ways that SIBO develops.