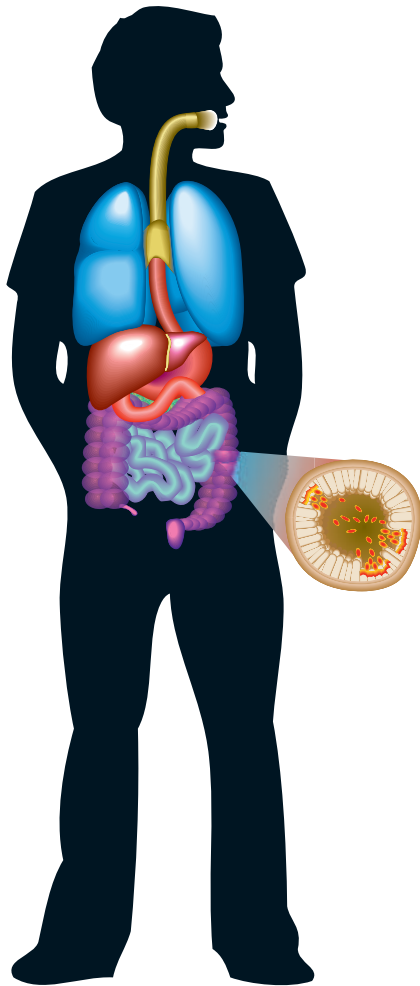
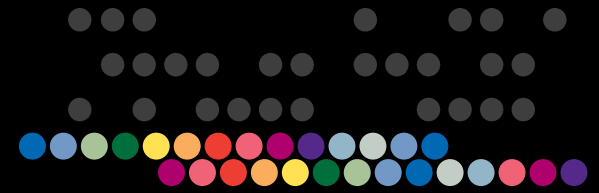


# Bacterial Overgrowth of the Small Intestine Breath Test



## Overview

Bacterial overgrowth of the small intestine is a serious digestive disorder that is treatable after proper diagnosis. Although widespread, it is frequently unsuspected in cases of chronic bowel problems and carbohydrate intolerance because its symptoms often mimic other disorders<sup>1</sup> (Table 1).

By inhibiting proper nutrient absorption, bacterial overgrowth of the small intestine can lead to systemic disorders such as altered permeability, anemia and weight loss, osteomalacia and vitamin deficiency.<sup>2</sup>

Bacterial overgrowth of the small intestine may also contribute to maldigestion and malabsorption. It frequently is a complication of parasitic infection. Patients with pancreatic insufficiency secondary to chronic pancreatitis are prone to developing bacterial overgrowth of the small intestine.<sup>3</sup>

The incidence of bacterial overgrowth of the small intestine increases with age, particularly in people aged 80 and older.<sup>4</sup> Elderly patients may develop malabsorption secondary to bacterial overgrowth. It has been suggested as the major cause of clinically significant malabsorption in the elderly and linked to the “failure to thrive syndrome” seen in older patients.<sup>2</sup>

## Causes of bacterial overgrowth

Normally, far fewer bacteria inhabit the small intestine than the ample growth found in the colon. Gastric acid secretion and intestinal motility keep the small intestine relatively free of bacteria. A wide range of abnormalities and malfunctions, however, can encourage bacteria to multiply in the small intestine (Table 2).

The most common causes relate to a decrease in the production of hydrochloric acid or pancreatic enzymes, thereby creating a unsterile environment for the small intestine.

Other causes of bacterial overgrowth of the small intestine include intestinal obstructions caused by Crohn’s disease, adhesions, radiation damage and lymphoma. Many years may pass between the development of diverticula and symptoms of bacterial overgrowth.<sup>5</sup>

### What this test does:

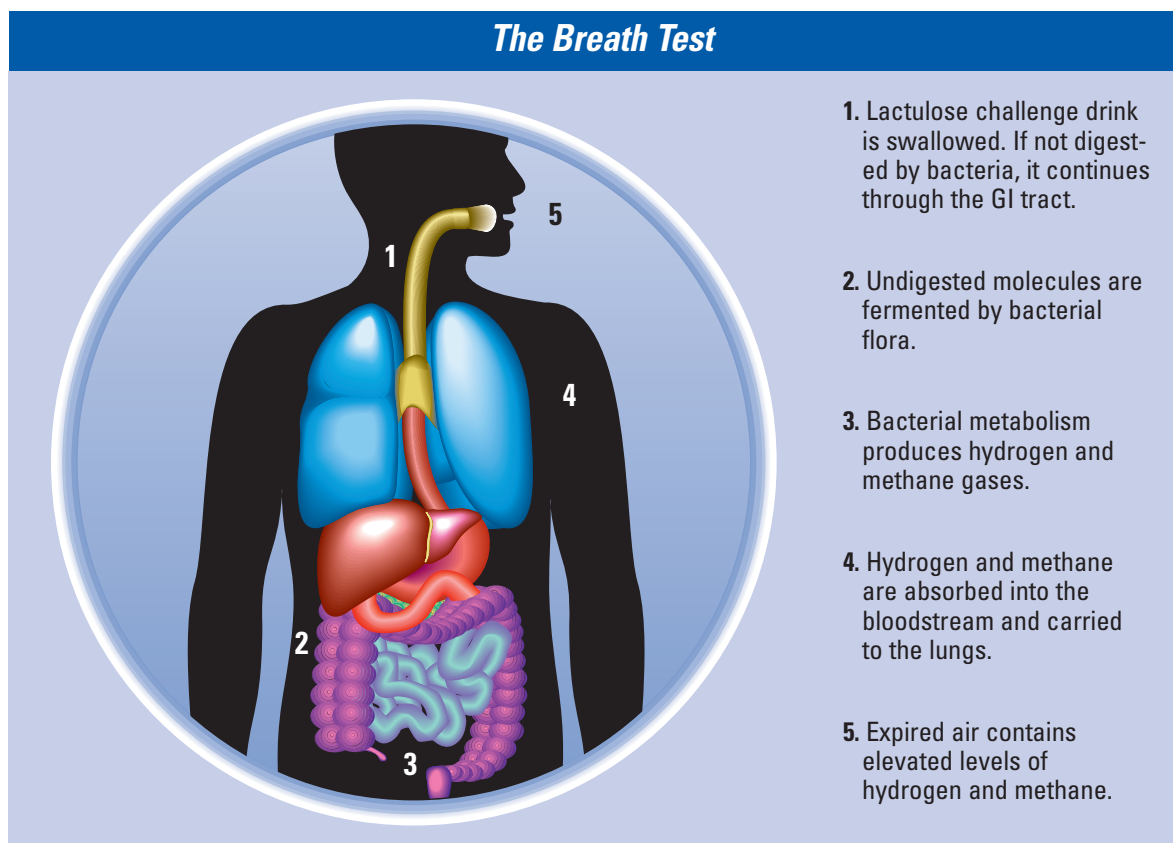
Accurately diagnoses an unsuspected cause of chronic bowel complaints.

Distinguishes bacterial overgrowth of the small intestine from other problems with similar symptoms.

Turn-around Time 10 days

## APPLICATION GUIDELINES

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## Effects on the body

Bacterial flora have the ability to act as small biochemical factories responsible for most of the effects of bacterial overgrowth of the small intestine. The flora contain very high concentrations of different enzymes which act upon substrates presented through the diet. Some of these enzymes produce toxic fermentation products normally not found in the small intestine.

Gut flora metabolize biliary steroids, which contribute to the diarrhea common in bacterial overgrowth and which may contribute to colon cancer.

*Overgrown flora in the small intestine can:*

- Inactivate pancreatic and brush border digestive enzymes due to production of proteases.
- Destroy dietary flavonoids, which serve as important natural antioxidants but are rapidly broken down and hydrolyzed by gut flora.
- Hydrogenate polyunsaturated fatty acids.
- Deconjugate bile salts.
- Consume vitamin B12.
- Produce vitamin B12 antagonists.
- Produce nitrosamines.

## Testing methods

While intubation and culture of intestinal aspirates have been the standard for determination of bacterial overgrowth of the small intestine, the method is invasive and assesses only one or a few sites, thus may lead to false-negative results. The less invasive alternative of breath trace-gas analysis has become widely accepted.

### Symptoms of Bacterial Overgrowth

- Abdominal cramps
- Bloating
- Diarrhea
- Gas
- Steatorrhea
- Vitamin B12 malabsorption and deficiency
- Weight loss

**Table 1**

Hydrogen/methane breath tests are simple to administer and offer greater patient comfort and convenience. In addition, these breath tests have good sensitivity and specificity.

### Challenge methods

Breath testing for bacterial overgrowth of the small intestine has utilized a number of different challenge substances, including lactulose, glucose, C-14D-xylose, and even rice flour, taken after an overnight fast. If bacteria exist in the small intestine, the bacteria will ferment the challenge substance and produce increases in breath hydrogen and methane that can then be measured in the laboratory to reflect the degree of bacterial overgrowth.

Lactulose is a synthetic disaccharide that is not absorbed by the intestinal lining and is only digested by intestinal bacteria. In the lactulose challenge test, patients collect a fasting breath sample, drink a 10 gm lactulose solution, and collect 5 more breath samples over the next two hours. Lactulose, as a challenge substance, offers a number of advantages over the other sugars:

- Unlike glucose, which is absorbed in the upper small intestine, lactulose is carried all the way to the colon, so can reflect bacterial overgrowth in the distal end of the small intestinal tract.
- Unlike glucose, lactulose is suitable for patients with diabetes, hypoglycemia and other blood sugar disorders, since the disaccharide is not absorbed by the intestine.
- Compared to glucose, lactulose is non-problematic for patients with yeast overgrowth.
- Unlike C-14 D-xylose, lactulose effectively reaches the terminal ileum and is not radioactively-labeled.

### Hydrogen and methane production

Both hydrogen and methane are end products of anaerobic microbial metabolism in the intestine. Because both gases may be produced in the intestine, testing for both hydrogen and methane is considered more sensitive than testing for hydrogen only.<sup>1</sup>

Research has demonstrated that individuals tend to preferentially produce hydrogen or methane.<sup>6,7</sup> Most methane in the gut is formed by the reduction of carbon dioxide and oxidation of hydrogen by methanogenic (methane-producing) bacteria.<sup>6,8</sup>

The factors influencing the production of methane are not been completely elucidated. Some studies have observed correlations between methanogenesis and slower transit time, alkaline fecal pH,<sup>9</sup> and even certain ethnicities (e.g. generally lesser amounts of methane production in Asians and higher amounts in Hawaiians and Caucasians).<sup>10</sup> Although one study has suggested that the presence of cancer in the large bowel may directly enhance methane production<sup>11</sup>, no correlation has been found between methane production and colon cancer risk among ethnic groups studied.<sup>10</sup>

Increased cramping and bloating has been observed in individuals producing more hydrogen and less methane following the ingestion of sorbitol or fiber, while high methane producers reported no increase in symptoms.<sup>12</sup> Similarly, more hydrogen than methane production has been noted in IBS patients compared to controls.<sup>13</sup> Methanogenesis also appears to be less prevalent in diverticulosis, Crohn's disease, and ulcerative colitis (UC).<sup>14</sup>

In anaerobic environments that are rich in dietary sulfate, sulfate-reducing bacteria may out-compete methanogens for hydrogen.<sup>15</sup> Interestingly, hydrogen sulfide (the product of these sulfate-reducing bacteria) has been linked with ulcerative colitis,<sup>16,17</sup> perhaps one reason for the reduced methanogenesis seen in this disorder. Bile acids, the major components of human bile, are capable of inhibiting bacteria, particularly

methanogens. Excess bile could result from bile malabsorption in disorders of the small intestine, such as Crohn's disease, or from ingestion of high fat diets. The latter might be one explanation for the finding that breath methane correlates inversely with obesity.<sup>8</sup>

More research is needed to establish correlations between various clinical disorders and the production of hydrogen versus methane. In the meantime, a measurement of total hydrogen and methane in the intestine can serve to evaluate the presence of bacterial overgrowth in the small intestine.

### Interpreting the results

#### Fasting baseline responses

The typical fasting breath sample contains less than 10 ppm of breath hydrogen or methane. A high breath hydrogen or methane level—one greater than 20 ppm—is likely to be found in patients with bacterial overgrowth. Methane, in particular, is likely to be produced by fermentation of brush border glycoproteins that are deposited into the gut lumen in individuals with bacterial overgrowth.

Fermentation of residual carbohydrate by oropharyngeal bacteria may also contribute to elevated levels of hydrogen. Rinsing the mouth with a chlorhexadine-containing mouthwash prior to breath collection can reduce this likelihood.<sup>18</sup>

#### Lactulose response

The Bacterial Overgrowth of the Small Intestine Breath Test using the lactulose challenge typically causes a two-phase response. During the test, hydrogen increases early as lactulose comes into contact with bacteria in the small intestine. This rapid response distinguishes bacterial overgrowth from normal colonic flora, which produce a later, more prolonged increase in breath hydrogen.<sup>1,19</sup> Genova Diagnostics' test monitors breath gas during the first two hours so colonic fermentation is either not detected or seen as a rise in the final breath specimens.

A breath hydrogen peak greater than 12 ppm above the fasting level within 30 minutes of ingesting lactulose and preceding the colonic excretion response by 15 minutes indicates bacterial overgrowth of the small intestine.<sup>1,19,20</sup>

#### False positives

The majority of false-positives reported in Bacterial Overgrowth of the Small Intestine Breath Test can be eliminated if patients follow proper instructions and preparation.<sup>1</sup>

*Typical problems include:*

- Eating high fiber foods within 24 hours of the test, which elevates the level of fiber in the colon at the beginning of the test and increases breath hydrogen production. No starches except rice should be eaten the night before the test. A protein and rice meal, such as beef, poultry, fish or tofu, should be eaten the night before. Fiber supplements should be discontinued 24 hours before the test.
- Smoking in the area of the test, which produces high hydrogen levels and unstable baseline results. Breath samples should not be collected where patients are exposed to tobacco smoke.
- Sleeping during the test, which increases both hydrogen and methane levels due to the slowdown in removal of breath trace-gases from blood.

#### False negatives

False negatives may result from any of the following:

- Severe diarrhea or recent use of an antibiotic, laxative or enema. Any of these may inhibit bacterial fermentation of carbohydrates and thus production of breath trace-gases.<sup>21-25</sup> Patients should wait at least one week following completion of antibiotic treatment or after recovery from severe diarrhea in order to reestablish colonic flora.
- Heavy concentration of sulfate-reducing bacteria in the intestine. Such organisms may outcompete methane-producing bacteria and consume hydrogen in the process of forming hydrogen sulfide (H<sub>2</sub>S). This may result in low amounts of both hydrogen and methane, despite the presence of bacterial overgrowth. Gas emissions in this

condition are likely to be sulfurous and foul-smelling (like rotten eggs).

- Bacterial overgrowth in the distal ileum. In this case, the peaks of hydrogen and methane may be obscured by the normal colonic peak.

Hyperacidic colon contents do not affect the lactulose challenge because the test reports bacterial fermentation in the small intestine, where the pH is more alkaline.

## Clinical therapeutics

Once bacterial overgrowth of the small intestine has been diagnosed, two steps are necessary:

1. Treat the overgrowth symptoms.
2. Investigate the underlying causes to keep bacterial overgrowth from recurring.

While tetracycline (250 mg four times daily) is the traditional antibiotic choice, research indicates that up to 60% of patients with bacterial overgrowth no longer respond to it.<sup>5</sup> Several broad-spectrum antibiotics have been used effectively. Augmentin (250-500 mg three times daily) is generally effective and well-tolerated. Acceptable alternatives include the cephalosporin Keflex (250 mg four times daily) and Flagyl (250 mg three times daily).<sup>5</sup>

Antimicrobials such as penicillin, ampicillin, neomycin, kanamycin and oral aminoglycosides are ineffective in treating bacterial overgrowth because of their poor activity against anaerobes. A nonabsorbable rifamycin derivative, Rifaximin, has been used effectively against anaerobic intestinal bacteria in Italy.<sup>26</sup>

Several natural antimicrobials may be useful in the treatment of bacterial overgrowth syndromes, although studies establishing their effectiveness against a broad range of anaerobic bacteria are lacking. Possible candidates include allium sativa (garlic), oil of oregano, Lonicera japonica (honeysuckle), grapefruit seed extract, forsythia suspensa, bismuth subsalicylate, and berberine sulfate or berberine-containing herbs: Hydrastis canadensis (goldenseal), Coptis chinensis (Coptis or goldenthread), Berberis aquifolium (Oregon grape), and Berberis vulgaris (barberry). Several herbal mixtures on the market, including some ayurvedic formulas, are thought to have strong broad-spectrum antimicrobial activity.

## Diet and Nutrition

A diet low in sugar and other carbohydrates, particularly disaccharides, may be helpful in reducing bacterial counts and associated symptoms. Disaccharidase enzymes are normally produced by the intestinal microvilli, allowing for complete carbohydrate digestion in the small intestine. Bacterial overgrowth in the small bowel may irritate the intestinal lining to the point of reducing this function. This results in increased substrate for the organisms, and further proliferation. Temporary restriction of disaccharides in the diet, including lactose, sucrose, maltose and iso-maltose (concentrated in grains), may serve to "starve" the excess bacteria and allow healing of the intestinal lining.<sup>27</sup> Permanent avoidance of lactose (or co-administration of lactase) is recommended in individuals known to be genetically lactose intolerant.

Nutrient insufficiencies should be considered in cases of significant bacterial overgrowth and malabsorption. In general, malabsorption can be attributed to intraluminal effects of proliferating bacteria combined with damage to the intestinal villi. Bacterial uptake of cobalamin (vitamin B12) prevents the vitamin from being absorbed by intestinal cells, possibly leading to pernicious anemia. Bacterial alteration of bile salts to free bile acids results in impaired micelle formation and fat malabsorption, including fatty acids and fat-soluble nutrients, such as vitamin K, A, D, and E.<sup>5</sup>

Intraluminal fatty acids may affect mineral metabolism by forming insoluble "soaps" with calcium and magnesium, thus making them unavailable for absorption.<sup>2</sup> Osteomalacia, night blindness, and even hypocalcemic tetany have been observed in some individuals with bacterial overgrowth-induced lipid malabsorption.

Hypoproteinemia may result from several factors, and is occasionally severe enough to cause edema.<sup>5</sup>

### *Causes of bacterial overgrowth of the small intestine*

- Achlorhydria, hypochlorhydria or drug-induced hypoacidity
- Crohn's Disease
- Diabetes mellitus
- Giardiasis and other parasitic infections
- Immunodeficiency syndromes (particularly sIgA)
- Intestinal adhesions
- Systemic lupus erythematosus
- Malnutrition
- Chronic pancreatitis
- Reduced motility in elderly patients
- Scleroderma
- Stasis due to structural changes — diverticulitis, blind loops, radiation damage

**Table 2**

## Bacterial Overgrowth of the Small Intestine Application Guide

### Treating underlying causes

Bacterial overgrowth of the small intestine may recur if the root causes are not eradicated (Table 2).

Two major factors control the concentrations of bacteria in the small bowel: gastric acid secretion and intestinal motility. Other controlling mechanisms include mucosal factors, immunoglobulins, an intact ileocecal valve, and the bacteriostatic properties of biliary and pancreatic secretions.<sup>5</sup>

Deficient production of gastric acid can result in maldigestion of food (serving as more substrate for the microbes), as well as increased survival and delivery of organisms to the small intestine. Correcting gastric acid production and/or betaine hydrochloride supplementation with meals will be helpful in these patients.

A sluggish digestive tract allows for excess proliferation of organisms. Addressing various causes of intestinal stasis will help to minimize this process. The addition of insoluble fiber will help to create bulk and encourage motility. Soluble fibers may be poorly tolerated until bacterial counts have been reduced.

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### How do I order this test?

For BOSI kits or information, please call a Client Services representative at 800-522-4762 or order online at [www.GDX.net](http://www.GDX.net).

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