

## Small Intestinal Bacterial Overgrowth-Symptoms, Diagnosis, and Treatment of Patients with Positive and Negative Results

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Good evening everyone, this is Martin Carr, and I am a gastroenterologist in Orange County, California, where I have been for just about 30 years helping people with everything from irritable bowel syndrome to inflammatory bowel disease and liver disease. In recent years have been focusing on trying to help patients with functional gut disorders and this evening I will be talking about something that we call small intestinal bacterial overgrowth or SIBO for short. You will see why being able to do a test for this has shown to be very helpful when we are trying to sort through the best way to help people with a very common set of symptoms of functional gut disorders. Patients who have small intestinal bacterial overgrowth may have intestinal bloating or excessive gas or flatulence. They may have abdominal pain, they may have diarrhea, or they may have severe constipation. That includes an awful lot of patients who are seen in gastroenterology offices and primary care offices all over the developed world. Let me first talk about the normal physiology of the GI tract with respect to bacterial populations and explain what is going on in people who have small intestinal bacterial overgrowth. In the normal circumstance, people have quite a lot of bacteria in the mouth but much less in the esophagus and in a normal person who produces stomach acid, there is very little in the stomach because the stomach acid makes the stomach inhospitable to bacteria. Then down in the duodenum, the first part of the small intestine, enzymes from the pancreas coming into the stomach is stimulated by the presence of food. Those enzymes will digest bacteria also. Bile is produced by the liver and is important for fat digestion and absorption and also absorption of fat soluble vitamins. Bile also will prevent bacterial growth in the small intestine under normal circumstances. In the small intestine there is a tremendous production of what is referred to as immunoglobulin A or IgA and that is the type of immunoglobulin that is active inside the chamber of the small intestine. That antibody is antibacterial and also keeps the bacterial count in the small intestine generally very low.

When special tests are done to actually get a little sample of fluid from the small intestine, the number of bacteria will be less than thousand per milliliter,

whereas in the normal colon it will be more than one billion per milliliter. So why does this become deranged and why do some people have small intestinal bacterial overgrowth? Many of the people have it because of small intestinal motility issues. People with irritable bowel syndrome can have abnormalities in the normal sweeping motions of the small intestine that clear the small intestine out while we sleep, and as a result they can gradually get increase in bacterial counts. They also may have subtle immunologic abnormalities in the gut that can allow bacteria to grow.

There are many other groups of patients who can have small intestinal bacterial overgrowth. For example, people who have chronic pancreatitis and don't produce enough pancreatic enzymes will not have those enzymes fighting off the bacterial growth in the small intestine. People with cirrhosis of the liver don't make as much bile and therefore can get small intestinal bacterial overgrowth. People with diabetes have neuropathy of the gut and also if the diabetes is not controlled well, will have more glucose in the liquid inside the intestine that can foster bacterial overgrowth. Another example of a disease that can lead to SIBO is scleroderma, which affects the muscles of the small intestine as well as other parts of the body including skin and lungs. When it affects the small intestine, it can cause a quite severe motility problem and result in very severe small intestinal bacterial overgrowth.

So what happens when the bacteria overgrow? Well, it varies. In the mildest cases these individuals are having competition between the bacteria in the upper small intestine and their own intestines and digestive system, and there is production of extra hydrogen, methane, sometimes other gases. These people may just have annoying symptoms of bloating or gas, looser stools after meals. But in more severe forms of small intestinal bacterial overgrowth, the growth and the numbers of bacteria can be some can become so excessive that the bacteria will be changing the nature of the bile and thereby preventing fats from being absorbed. The bacteria can also compete for intake of vitamin B12, one of the essential B vitamins that is important for our nerves and brain and making blood cells. The bacteria can also disrupt carbohydrate digestion and lead to production of short-chain fatty acids. The bacteria can also have an inflammatory effect and actually cause some damage to the lining of the small bowel and make it difficult to absorb short-chain peptides and amino acids. So in the most severe cases there is malabsorption of fat, poor digestion of carbohydrates and protein.

Vitamin B12 deficiency, thiamine deficiency, niacin deficiency and iron deficiency as well as deficiency of fat soluble vitamins, for example vitamin D, can occur. These people can develop significant weight loss and can be quite ill, not just experiencing some unpleasant excessive gas or bloating or looser stools.

There is a very important test available to diagnose small intestinal bacterial overgrowth. Fortunately, we don't have to slip a tube through the nose, down into the stomach and intestines and aspirate liquid in a careful fashion, to make this diagnosis. Instead, we can do something called a lactulose breath test. At the medical center I work at in Fullerton, California, we have recently been able to start doing this test because a grateful patient donor paid for us to get the Quintron BreathTracker and associated supplies and materials and a laptop to be able to provide this test. In this test the patient has to avoid eating sugars and carbohydrates and have a very restricted diet of rice and chicken the night before the test and then fast after midnight. At our institution they come in at about noontime, having had water that morning but no food, and then will be given a cup of water that has 10 g of lactulose, which is a sugar that we humans cannot digest or absorb. But bacteria can easily metabolize lactulose and they turn it into hydrogen, and if there are methane-producing bacteria present also, that hydrogen will be turned into methane. Now, this will happen with anyone in 3 hours or more after the lactulose would get all the way through the small intestine into the colon, but in people with small intestinal bacterial overgrowth, they will start having metabolism of the lactulose and production of hydrogen or methane within 90 minutes of taking that lactulose dose. So in the test the patient is breathing through a little tube that has a bag keeping some air in a reservoir for a moment as we use a syringe to take a sample and every 15 minutes we do another reading. Usually the patient is there for about 2 hours doing the test and then we have the results. We know if they have small intestinal bacterial overgrowth or not.

The next step is then to treat it. For people who have just a hydrogen overproduction there is an antibiotic called rifaximin or brand name in the United States XIFAXAN and that can be given 550 mg 3 times a day for 2 weeks with a fairly good eradication, I should say reduction of the bacteria not eradication. Then typically anywhere from 2 to 4 to 6 months the problem will typically come back, although in a moment I will talk about some things that can be done to make that less likely. Now if methane is what is being overproduced by small

intestinal bacterial overgrowth, it's necessary for both Xifaxan or rifaximin and also another antibiotic, usually neomycin 500 mg, twice a day for 2 weeks along with the Xifaxan to reduce that combination of bacteria that are producing the methane. Typically the methane spike patients have abdominal discomfort, bloating, but also constipation.

A very interesting paper from 2014 talked about another way of treating small intestinal bacterial overgrowth and that is with herbal therapy. The title of this paper was Herbal therapy is equivalent to rifaximin for treatment of small intestinal bacterial overgrowth and the first author was Victor Chedid, M.D. and this was published in May, 2014. This was based on treatment of patients at Johns Hopkins in Baltimore. In this study, patients over a 4 year period were able to choose either the standard treatment with rifaximin 400 mg 3 times a day for 4 weeks, not 2 weeks, or a mixture of 4 different herbal preparations of which they would take 2 capsules each twice a day. That 30 day supply costs about \$120 (much less than Xifaxan for some patients). The results were quite impressive. The patients receiving herbal therapy had a negative lactulose breath test, that is they converted from positive lactulose breath test to negative test or normal 46% of the time after the 4 weeks of treatment, whereas patients who got the 4 weeks of rifaximin only had 34% negative lactulose breath tests, although that was not statistically significantly different. Then the rifaximin failures were treated further. Fourteen of them were given that same herbal therapy and 57% of those rifaximin failures could then be converted to a negative lactulose breath test with the herbal treatment. Ten patients were given a quite powerful triple antibiotic treatment for 4 weeks--they also converted to negative breath test 60% of the time but had lots of side effects. Even just the rifaximin in this study give adverse effects 9% of the time. In one case a patient developed C. difficile colitis, a quite serious condition that requires special treatment on its own and causes severe diarrhea. Two other non-C. difficile diarrhea cases occurred. Whereas in the patients getting herbal treatment there was only 1 case of diarrhea and it was not C. difficile.

The group at Johns Hopkins felt that this herbal therapy is a definite alternative to the rifaximin and might have the advantage of not affecting the gut flora as much and putting people at risk of C. difficile colitis. What about people who do not have success with the antibiotic or herbal treatment or any other treatments? There is one other treatment that is available, which is to use what is called an

elemental diet. This is a mostly liquid diet that is composed of a digested set of nutrients, very small carbohydrate molecules, partly broken-down proteins and triglycerides and easy-to-digest other fat-related sources of nutrition and vitamins that doesn't necessarily taste all that good unless there is some care taken to flavor it. It means being on a liquid diet for a month or more. There is a good conversion rate to negative breath test or resolution of the bacterial overgrowth in people who have an elemental diet, but you cannot live on an elemental diet forever.

What other things can be done to keep small intestinal bacterial overgrowth from coming back? Again, there does not seem to be a perfect cure. One of the options potentially is for people to be on a low FODMAP diet. I've referred to low FODMAP diets, which were first popularized by the group at Monash University in Melbourne, Australia, and there is further information about that elsewhere on my website [MartinCarrMD.com](http://MartinCarrMD.com). That is basically a diet that eliminates some of the types of small molecules, mostly carbohydrate-related, that can be difficult for people to digest and could potentially cause bacterial overgrowth. Although it is still controversial whether low FODMAP diets could be a primary treatment for small intestinal bacterial overgrowth, in my experience with patients who reduce their sugar and carbohydrate dietary intake after being treated for small intestinal bacterial overgrowth, it does seem to help to slow the return of that problem.

There is another approach that has been used at a number of institutions. It was first developed as a concept at Cedars-Sinai Medical Center under the direction of Mark Pimentel and his GI motility group there, and that is to use a very small dose of erythromycin, about 75 mg, at bedtime. Erythromycin is an antibiotic that years ago was popular for use treating strep throat but not really any other kind of infection. It has a very narrow bacterial spectrum and really does not affect the GI tract flora much at all. So it is actually safe to use for its other purpose, which is as a motility drug. Erythromycin stimulates the motilin receptors in the gut and so people who have irritable bowel syndrome or scleroderma or have diabetes and gut neuropathy might have improvement in that overnight small intestinal pattern of sweeping contractility that keeps the small bowel clear by taking a small dose of erythromycin at bedtime.

It's also been said that eating many small meals and snacks throughout the day might be a factor in contributing to small intestinal bacterial overgrowth in some people. Dr. Pimentel, on his Twitter feed, has mentioned that he thinks that patients with SIBO should learn to eat only 3 meals a day and give periods of fasting in between those meals to allow the small intestine to go through its cleanout period when contractile waves wipe everything down toward the colon, and that that may be helpful as well. Whether there is a possibility of ongoing herbal treatments has not been studied or reported yet but that is possible. There are some patients with SIBO who have to have recurrent antibiotic treatment and may have to take the rifaximin multiple times per year. Other antibiotics are sometimes used if the rifaximin is not successful, but again, it is not clear whether repeated long-term antibiotic treatment would definitely be safe over many, many years.

What about people who have the lactulose breath test and are negative, what do we do with them? We just talked about what to do with people who are abnormal for that lactulose breath test, who have an early hydrogen or methane peak, but what about many patients, at least half of irritable bowel syndrome patients, who are negative when they have a lactulose breath test? For those patients there are many other things to do. Elsewhere on my podcast series and on my website we discussed the IBS Simpler Solutions handout which helps the patient figure out their dietary triggers. This is distinct from and a first step before actually going through a somewhat more complex low FODMAP diet. A low FODMAP diet can definitely be helpful in people figuring out what is causing their IBS symptoms.

People who have bloating or flatulence or abdominal pain or loose stools after meals and have had a workup that shows that there is not some other cause but that it really does seem to be from functional gut disease or irritable bowel syndrome can benefit from use of peppermint products and use of ginger and use of fennel or combinations of any 2 or 3 of those. Medications by prescription called dicyclomine or hyoscyamine can relieve cramping, although dry mouth can be a side effect of those medications. Then there are neuromodulators including the medication amitriptyline and related tricyclic medications. Another neuromodulator for IBS symptoms is mirtazapine. Also important to mention is stress reduction therapy, for example, mindfulness-based stress reduction, which is a well-established effective 8 week course based on the very important work in

this area by Jon Kabat-Zinn at the University of Massachusetts starting in the 1990s. Those courses are available in any medical centers around the country and in Europe. Cognitive behavioral therapy, which is more of a one-on-one interaction between a psychotherapist and a patient, can also be very helpful in identifying the catastrophizing or negative behavior patterns that patients with IBS and repetitive symptoms can get into. Patients can be very anxious and fearful about situations that they think will make it hard to deal with the symptoms or that are likely to make the symptoms worse. Cognitive behavioral therapy helps patients to study that. There is an excellent book called Reclaim Your Life from IBS by Melissa Hunt, a psychologist at the University Pennsylvania, that is meant to help an individual go through a set of homework assignments to in a sense give themselves cognitive behavioral therapy in a stepwise fashion. I have had several patients benefit from the approach in her book. So there are many approaches and in my office in Fullerton, California, I am trying to do more and more organization to help patients with irritable bowel syndrome get the best diagnostic workup and best treatment in a comprehensive, integrative medicine or holistic medicine point of view. We will keep trying to improve things for everyone there. I hope that you have enjoyed listening to this podcast segment. There will be a transcript of it up on my website [MartinCarrMD.com](http://MartinCarrMD.com) and there will also be a link to that article about herbal treatment for small intestinal bacterial overgrowth as part of the transcript on the website. Good luck everyone. It is a rainy, somewhat cold weekend here in southern California. Hopefully we will get more rain this winter and spring, we need it. Good luck to the rest of you in the United States, and wherever else you may be listening, the rest of this year. I look forward to speaking with you again on another podcast segment, good night.