



## Probiotics, Prebiotics, and the Microbiome

### The Microbiome

Did you know that all multicellular organisms, including every animal and plant, are covered in a vast array of microorganisms? Microorganisms, also known as microbes, are extremely small (microscopic), living organisms, such as bacteria, viruses, yeast, parasites, and more. They live on our skin, in our body fluids, and throughout our digestive tract in large quantities and varieties. The moment we are born, we encounter countless microorganisms. The number of single-celled organisms on and within you is greater than the number of cells that make up your own body. This collection of microorganisms, which is unique to each individual, is their microbiota. The collection of the genetic information from all these microorganisms in a specific environment is referred to as the microbiome. Different parts of the body, for example the skin or the intestinal tract, have their own microbiomes and microbiota.

The gut microbiome is exceptionally diverse, with estimates of 100 trillion microorganisms, from 500-1,000 different species! Despite these vast numbers and varied species there is a fine balance. We have co-evolved with these microorganisms – we give them a place to live and food to eat and they help support our overall health. They produce certain vitamins and short chain fatty acids, interfere with the growth of harmful

There are just as many, if not more, microorganisms living in your digestive tract and on your skin as there are cells in your body!

bacteria, modify the immune system, and improve our health in ways researchers are only beginning to study.

### Microorganisms and Our Health

While the term ‘microorganism’ refers to all types of microbes, we are going to focus primarily on bacteria. When we think about the bacteria that colonize, or live in, our intestinal tract, we typically sort them into two categories: beneficial strains of bacteria (non-pathogenic), including those in the genera *Bifidobacterium* and *Lactobacillus*, and potential disease-causing strains of bacteria (pathogenic), including enteropathogenic (EPEC) and enterohemorrhagic (EHEC) *Escherichia coli*, *Shigella*, and *Clostridioides difficile*. While it’s much more complex than this, it is an easy way to sort which bacteria will generally improve our health or harm us. Beneficial bacteria keep pathogens in check and offer many health benefits. Disease-causing bacteria release proteins and toxic by-products that can cause inflammation and harmful symptoms such as diarrhea. Some, such as *Helicobacter pylori*, can be both beneficial in certain quantities and harmful in other quantities.

The balance between beneficial and harmful bacteria is important for maintaining health. The diversity, or different types of microorganisms, of our gut microbiome is critical – greater diversity allows our gut to be resilient and bounce back from any disturbances to the balance. Several factors can upset this balance, including diet, stress, hygiene, and medications, particularly antibiotics. Dysbiosis occurs when there are shifts in the balance of the microbiota.

However, at this time, we don’t have any good ways to

measure or analyze the gut microbiome of the average person going to their physician to get help for digestive symptoms. While some practitioners might offer breath tests that look for metabolites of certain bacteria, these aren't helpful in most cases.

## Modifying the Microbiome

There are many ways to treat and manage dysbiosis. In cases of bacterial infection, antibiotic treatment might eradicate the offending bacteria. When the problem is ongoing, probiotics and prebiotics can help return balance to the microbiome. An additional strategy is microbiota restoration or adding back bacteria to help improve an individual's microbiome. In this section, we will explain how we can use these tools to affect the gut.

### Probiotics

Canadian laws specify that a probiotic product must contain live microorganisms that research shows to be beneficial, in adequate amounts to confer a health benefit. You will most often find probiotics in the form of supplements, but some foods also contain probiotics (not to be confused with fermented foods; see below). Typically, an approved probiotic will contain a limited variety of beneficial bacteria, sometimes a few strains and sometimes just one. However, the strain(s) will be a type of bacteria (or other microorganism) that research studies show to be effective for treating a specific ailment. The live bacteria populate the gut and help improve the balance in the microbiome, as well as exert specific effects.

Bacteria from the *Bifidobacterium* and *Lactobacillus* genera can improve health in many ways, but different strains can exert different effects. For example, research shows that *Bifidobacterium infantis* 35624 (Align®) can improve abdominal pain, bloating, and gas in those who have irritable bowel syndrome (IBS). This probiotic is an effective option for individuals with these specific symptoms, but it might not be helpful for someone with a different set of symptoms or benefit someone with no digestive troubles.

Some other benefits of various strains of *Bifidobacterium* might include reducing post-antibiotic diarrhea, reducing the risk of necrotizing enterocolitis in infants, reducing symptoms

### Beneficial Bacteria vs Probiotic

There are many bacteria that live in/on us that can be beneficial to our health, but this does not make them probiotics. Probiotics are products that contain specific strains of bacteria in adequate quantities for which there is evidence showing its efficacy at treating a specific condition.

## Key Definitions

**Microbiome:** the aggregate of microorganisms, their genetic information, and the conditions of the environment they are in (such as the intestinal tract)

**Microbiota:** the microorganisms that inhabit a specific environment (such as the intestinal tract)

**Microorganism:** a very small (microscopic) organism, such as a bacterium, virus, or yeast

**Microbe:** another term for a microorganism

**Dysbiosis:** the disruption of the composition and/or diversity of the microbiota

**Antimicrobial (Antibiotic):** a medicine that either inhibits growth of or destroys microorganisms

**Probiotic:** live microorganism (usually bacteria) administered with the purpose of improving health

**Prebiotic:** a component of food that humans can't digest but that feeds beneficial bacteria in the gut

**Postbiotic:** metabolic by-product of probiotics

in inflammatory bowel disease, preventing the growth of harmful bacteria, and improving colon regularity. Many strains of *Lactobacillus* offer similar potential benefits, including managing diarrheal conditions in children, improving blood lipid levels, preventing urinary tract infections in women, and treating inflammatory bowel disease.

While most probiotics use beneficial bacteria, some products focus on other microorganisms, such as Florastor®, which uses a yeast known as *Saccharomyces boulardii* lyo CNCM I-745. Florastor® is especially useful at preventing antibiotic-associated diarrhea, since the yeast is not killed by antibiotics.

It can be difficult to find a probiotic since there are so many products and most studies on them are small. In addition, there is little oversight in the marketing of these products, so the claims on them might not be validated or important. For instance, many products focus on the number of organisms in a dose, which might lead you to buy the product with the highest number, but this might not be the best product for you. However, there is some research that can help you find a product that meets your needs.

Before taking a probiotic, speak with your healthcare team and make sure that there is evidence that the specific strain you wish to take may be beneficial for you. Also, a trusted group of experts has created an evidence-based guide on probiotic products available in Canada that can support you in your care. The Alliance for Education on Probiotics (AEProbio) is an international collaboration of doctors, researchers, and scientists

working together to promote the clinical use of probiotics for better health outcomes. Each year, they conduct an unbiased review of the available scientific evidence on probiotics to update the *Clinical Guide to Probiotic Products Available in Canada*, available at [www.probioticchart.ca](http://www.probioticchart.ca).

### Prebiotics

While the most obvious way to increase the number of beneficial bacteria in your gut is to take a probiotic, you can also feed the good bacteria already in your gut so that they reproduce and populate a higher proportion of your microbiota. There are certain carbohydrates in our food that we cannot digest, which we call fibre. There are many types of fibre in our food, and helpful bacteria love to chow down on some of them. These special fibres are prebiotics. The most well known and extensively studied prebiotic is inulin, a type of fructo-oligosaccharides (FOS) found in plants such as chicory, whole grains, onion, garlic, asparagus, banana, tomatoes, and Jerusalem artichokes, among many others. Chicory is sold commercially as Benefibre® (inulin), although there are other types as well. Galacto-oligosaccharides (GOS) are plant sugars linked in chains found in breast milk and fermented dairy products, beans, and certain root vegetables.

When you eat these foods, the prebiotics stay intact through the stomach and small intestine, then bacteria in the large intestine break the fibres down (fermentation) and use them as fuel. This allows the bacteria to reproduce, leading to larger colonies of good bacteria.

#### Increase Your Prebiotic Intake by Adding These Foods to Your Diet:

- Jerusalem artichokes
- bananas
- artichokes
- tomatoes
- leeks
- onions
- garlic
- chicory root
- whole grains (oats, wheat, barley, etc.)
- legumes (beans, lentils, soy, etc.)
- nuts & seeds (almonds, flax, etc.)



Make sure to increase your prebiotic intake gradually, since sudden changes in the quantity of fibrous foods you eat can cause bloating, abdominal pain, and other digestive symptoms.

### Fermented Foods

Many people mistakenly claim that fermented foods, such as yogurt and sauerkraut, contain probiotics. As we discussed earlier, probiotics are products that must contain a certain amount and type of live bacteria, based on scientific evidence for certain conditions. Fermented foods contain the microorganisms that initiated the fermentation. However, the strains of bacteria that these products contain can be variable, and they may or may not still be active by the time they reach your intestinal tract. For these reasons, eating fermented foods is a less reliable way of increasing the populations of beneficial bacteria in the gut than taking probiotic supplements.

While the microbe content of fermented foods isn't guaranteed, they are safe in most cases and might offer benefits. If it works with your dietary routine, adding in foods such as yogurt, kefir, sauerkraut, kimchi, and kombucha can be a nice accompaniment to any probiotics you might take to treat digestive diseases and disorders. However, if you are immunocompromised (common in individuals who take corticosteroids, biologics, or immunosuppressive medicines to treat Crohn's disease and ulcerative colitis), you should speak with your doctor before eating fermented foods, as it is harder for your body to fight off any bad bacteria that might be in these products.

### Postbiotics

Most of the beneficial effects of bacteria in the gut don't come from the microorganisms themselves, but rather from their metabolic by-products (waste). When bacteria eat, they produce waste, and while it might sound gross, these waste products can help us. For example, when bifidobacteria eat fibre, they produce short-chain fatty acids, which our bodies use to improve immune function and strengthen the intestinal barrier.

Some researchers have been looking at these end-point products and considering the possibilities of delivering them directly to the gut. This might offer a way to bypass the complication of getting living organisms into the gut unharmed, and instead provide the benefits directly. In addition, this could be a way for individuals who are immunocompromised to obtain the benefits of probiotics.

### Antibiotics

You are probably very familiar with antibiotics. If you've ever had a bacterial infection, your physician likely prescribed one of these, such as amoxicillin, to kill off the offending

bacteria. While antibiotics kill the bacteria that are causing you to be sick, they also kill helpful bacteria. This can cause other infections, because there aren't enough good bacteria to balance out harmful microorganisms. For instance, yeast infections and *Clostridioides difficile* (*C. difficile*), formerly known as *Clostridium difficile*, infection often occur after taking antibiotics. In some cases, *C. difficile* infection recurs, and may continue to recur, because the microbiome is imbalanced to the point that it is unable to restore itself.

Occasionally, taking probiotics after a course of antibiotics might prevent further damage to the microbiome by repopulating it in a beneficial manner. However, in many cases it is unnecessary and might make it take longer for the microbiome to recover.

Not all antibiotics are created the same, there are types available now and in development that target specific bacteria rather than the entire microbiome. One such example is rifaximin (Zaxine®), which is a treatment available for IBS and hepatic encephalopathy that targets harmful bacteria in the gut, with less impact on the beneficial ones.

### Microbial Restoration

The aim of microbiome restoration is to repopulate a diverse gut microbiota to treat disease, such as recurrent *C. difficile* infection. One approach is fecal microbiota transfer, or FMT, which is the transfer of fecal matter from a healthy donor into the intestinal tract of a recipient. There are many ways to perform FMT, including enema, colonoscopy, or oral capsules. Following transplantation, healthy bacteria begin to grow in the recipient's intestinal tract, reversing dysbiosis and preventing further *C. difficile* recurrence.

There are also several commercial microbiota restoration products in development. These products, similarly to FMT, aim to repopulate the diverse gut microbiota to treat disease. They have been initially studied in recurrent *C. difficile* and aim to provide safe, efficacious, Health Canada-approved microbial restoration. Products may be available in the next couple of years.

Dysbiosis of the gut microbiota has also been associated with a range of different GI and non-GI diseases such as IBS, inflammatory bowel disease (primarily Crohn's disease and ulcerative colitis), obesity, colon cancer, asthma, diabetes, neurological disorders, cardiovascular disease, and autoimmune conditions. Researchers have also been looking at the impact of FMT and microbial restoration on outcomes in these diseases.

### What to do With This Information

Before taking a probiotic, talk to your doctor about which specific products would be best for you. Your ideal probiotic(s)

will depend on your digestive health, which diseases you do or don't have, your diet and lifestyle, and many other factors. For example, the bacterial strains that work well for someone with constipation-predominant irritable bowel syndrome are likely different than the ones that help someone with Crohn's disease. For most people, eating fermented foods and prebiotics can help improve digestive health. Just make sure to slowly add in these foods by starting small and adding more as you can tolerate, and then follow our tips for being a good microbe host.

If you have long-term dysbiosis (e.g., if you have recurrent *C. difficile* infection) and are interested in microbiota restoration, talk to your doctor. They may refer you to a specialist who can best assess your condition and suitability of treatment.

## Benefits of Good Bacteria

The beneficial bacteria that populate the digestive tract work in many possible ways, depending on the type of bacteria and other factors, including:

- protecting against harmful bacteria
- regulating the responses of the immune system
- strengthening the tissue of the bowel wall
- helping to digest food
- producing vitamins such as thiamine, riboflavin, vitamin B12, and vitamin K
- enhancing absorption of some minerals
- improving symptoms of some digestive diseases and disorders
- helping to regulate weight
- improving heart health

## Be a Good Microbe Host

- eat plenty of fibre
- consume a wide variety of plant foods
- consume fermented foods
- reduce consumption of processed foods high in fat and sugar
- avoid overuse of antibiotics, if possible
- spend time in nature
- don't overuse hand sanitizer
- don't smoke
- get plenty of sleep and exercise

