

The Gut Microbiome in Covid-19

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I have been researching the interaction of the gut microbiome with Covid-19 since the start of the pandemic. Now that concrete information is available, I am incorporating this information into my CORONAVIRUS GUIDE, which I update periodically, but I believe the information is so important that I am posting it as a separate document.

It's become clear that the impact of Covid-19 on the GI tract, even in people without digestive symptoms, can determine the outcome of severe infection and the risk of long covid or post-covid symptoms. Impairment of cognitive function and memory, one of the most frequently reported long-term complications of Covid-19, is strongly influenced by the health of your gut microbiome.

The science is complex, but it leads to specific recommended actions, which come at the end of this section.

Your body teems with microbes, tens of trillions of them. Collectively they are called the microbiome. They include bacteria, viruses, fungi, and –for most people in the world—worms and protozoa, like amebas. Bacteria have been the most studied; 99% of them are found in your large intestine. Because two-thirds of your lymphocytes make their home in the small intestine, there has been extensive investigation into the cross-talk between gut bacteria and immune function.

A lot's been published on the impact of gut bacteria on respiratory health¹ and on viral infections², so the early months of the pandemic saw considerable speculation about a link between gut microbes and Covid-19. Actual evidence began to emerge by the end of 2020. It derives from studies of patients in hospital and the numbers are small, but it presents a coherent picture.

First, people hospitalized with Covid-19 show profound changes in the microbiome as measured in stool specimens. Some of these changes may represent the impact of hospitalization, but there is a deeper connection. ACE2, the cellular receptor for the virus, has a special function in the small intestine. It acts as a chaperone for an enzyme that transports amino acids into the body. Damage to intestinal ACE2 creates amino acid deficiencies that impair gut immunity and barrier function³, producing abnormalities in the microbiome (this state is called *dysbiosis*) and increased permeability of the intestinal lining (the so-called “leaky gut.”)⁴. Intestinal leakiness in Covid-19 is associated with damage to the heart⁵.

Within the microbiome, Covid-19 decreases diversity and richness of gut bacteria, with depletion of some beneficial species and overgrowth of others considered undesirable⁶. What's lost, in particular, are bacteria that synthesize an important substance called butyrate (or butyric acid), a short-chain fatty acid that nourishes the cells of the large intestine. Butyrate is rapidly absorbed into your body, where it has anti-inflammatory effects, and enters your brain, where it supports the production of a protein called BDNF (brain derived neurotrophic factor), which helps your brain recover from injury^{7 8}. Covid-19 is associated with a decrease in levels of BDNF as measured in blood⁹.

Covid-19 also increases the richness of yeasts and fungi in the gut (the mycobiome)¹⁰. The predominant fungal opportunists promoted by Covid-19 are the well-known yeast, *Candida albicans*, its scary cousin *Candida auris* (which has received global attention as an invasive drug resistant species¹¹), and the potent allergen, *Aspergillus flavus*. These organisms persist in stool even after respiratory symptoms have cleared and nose or throat swabs show no active viral infection.

To date, no one has studied the impact of fungi in covid longhauers, but I've been investigating, treating and teaching about yeast and fungal overgrowth for over 40 years and I've seen what they can do. Intestinal fungi can exert potent, often undesirable, effects on immunity, inflammation and metabolism that create symptoms in many body systems. Stool testing for bacteria and yeast should be considered in all people with persisting post-covid symptoms.

Some researchers have found a correlation between specific bacterial disturbances and severity of Covid-19. Two provocative findings have appeared. First, severity correlates with lower levels of a key anti-inflammatory species and butyrate producer called *Faecalibacterium prausnitzii*. Loss of *Faecalibacterium prausnitzii* and its friends, the Bifidobacteria, persists for weeks after hospitalization, and correlates

with increased severity of systemic inflammation^{12 13}.

The largest study yet, from the University of Massachusetts, found that excessive growth of one species, *Enterococcus faecalis*, in fecal or oral specimens, was the best predictor of severe disease, more accurate than symptoms or underlying medical conditions¹⁴. The study's authors note that *Enterococcus faecalis* is a potent stimulator of inflammation. They believe it actively contributes to worse outcomes for people with Covid-19. Theirs is a reasonable theory, because the use of *Enterococcus faecalis* as a probiotic provokes the release of gamma-interferon¹⁵, a major driver of the cytokine storm of severe Covid-19 (This role of gamma-interferon is described in the CORONAVIRUS GUIDE, section on IMMUNITY).

Possible support for the importance of the oral microbiome in Covid-19 comes from a study done in Bangladesh¹⁶. In a randomized controlled study, these researchers had patients newly diagnosed with Covid 19, who chose to avoid hospitalization, use a povidone/iodine mouth wash (plus a nasal wash and eye drops) or use only warm water to flush their mouth, nose and eyes. Over a period of 4 weeks the need for oxygen therapy and for hospitalization was reduced 84% in the group using iodine compared to the group using water and the death rate was reduced by 86%. The researchers attributed the benefits to killing of the SARS-CoV-2 virus in the nose, mouth and throat, but by the time they were treated, these patients were already infected and already had symptoms, making it likely that the virus had already spread. Povidone/iodine kills bacteria as well as viruses and is quite effective at killing *Enterococcus faecalis* and other oral pathogens, so it is possible that eliminating pro-inflammatory bacteria from the mouth improved the outcome of disease in their patients.

So, here's the good news:

If an unbalanced microbiome increases susceptibility to more severe or prolonged Covid-19, restoring balance can lead to milder disease and reduce the impact of longhaul covid. There are several natural substances and dietary factors that can correct the specific microbiome imbalances described in Covid-19.

Resveratrol, a polyphenol that enhances activity of ACE2, inhibits the growth of *Enterococcus faecalis*^{17 18} and **curcumin**, another natural ACE2 enhancer, decreases bacterial virulence by breaking up biofilms that support the growth of *Enterococcus faecalis*^{19 20}.

Ursolic acid is a dietary compound found in many fruits, vegetables, herbs and spices and is used as a muscle-building supplement by body builders. Like resveratrol and curcumin, ursolic acid has anti-inflammatory, anti-viral and cancer-fighting activity²¹ and also inhibits the growth of *Enterococcus faecalis*²².

Dietary sources of ursolic acid include apple peel, cranberries, bilberries, blueberries, prunes, peppermint, rosemary, oregano, thyme, sage, and marjoram. Dried cranberries are an especially good source²³. Human clinical trials of ursolic acid show anti-inflammatory effects at doses of 150 mg taken 1 to 3 times a day^{24 25}. Ursolic acid may also inhibit the SARS-CoV-2 main protease^{26 27}.

Just as nutritional strategies can control colonization with the inflammatory organism *Enterococcus faecalis*, they can support growth of the anti-inflammatory *Faecalibacterium prausnitzii*, which is fed by fiber-rich foods, fiber supplements^{29 30}, and certain prebiotics³¹. Daily consumption of chick peas³² or of avocados³³ increases abundance of *F. prausnitzii* in human volunteers.

Although probiotics based on *F. prausnitzii* do not exist, two commercial probiotics can increase its levels, according to human clinical trials. *Bifidobacterium longum* BB536 increases the growth of *F. prausnitzii* at the same time it relieves symptoms of pollen allergy in adults³⁴ or upper respiratory infection in young children³⁵. *Bacillus coagulans* GBI-30, 6086 [GanedenBC(30)] was shown to increase growth of *F. prausnitzii* in men and women over the age of 65³⁶. *Bacillus coagulans* pre-treatment also enhanced the effect of prebiotics stimulating growth of *F. prausnitzii* in a clinical trial of older adults.³⁷

The bottom line:

A protocol for building a Covid fighting microbiome fits seamlessly into the program I call INTEGRATED VIRAL MANAGEMENT, described in the CORONAVIRUS GUIDE. These are the components:

1. **Diet:** a whole foods, plant-based diet, rich in vegetables, fruits, and spices to supply fiber, prebiotic carbohydrates, and polyphenols. Emphasize natural food sources of ursolic acid and rosmarinic acid like berries, especially cranberries, whole apples, prunes, peppermint tea, and savory herbs like rosemary, oregano, thyme, sage and turmeric. In a large, well-done study of health professionals in 6 countries, scientists from Johns Hopkins, Stanford, Harvard and Columbia found that eating a plant-based diet of this type significantly reduced severity of Covid-19³⁸. In fact a 40% increase in consumption of vegetables created a 72% reduction in the risk of developing moderate to severe disease, as opposed to minimal or mild disease.
2. Supplement with resveratrol and curcumin (more about these in ACE2 ENHANCEMENT and THERAPEUTIC PROFILES in the CORONAVIRUS GUIDE). Randomized

controlled clinical trials from India³⁹ and Iran⁴⁰ have demonstrated that curcumin supplementation significantly improves the outcome of people with Covid-19.

3. Take a probiotic shown to enhance the growth of *Faecalibacterium prausnitzii* like *Bifidobacterium longum* BB536 or *Bacillus coagulans* BC-30 (Schiff Digestive Advantage is one product). Add prebiotics that stimulate bacterial production of butyrate, like fructooligosaccharides (FOS) or galactooligosaccharides (found in Bimuno and Hooligos). Or you can supplement directly with sodium butyrate 500 mg 3 times a day.
4. If you develop acute symptoms of Covid-19, supplement with ursolic acid 150 mg 3 times a day and use an iodine-based mouthwash (don't swallow, rinse for 30 seconds and spit it out). The study from Bangladesh used a preparation of standard povidone/iodine 10% (available online and in pharmacies) and diluted it with water to produce a concentration of 1% povidone iodine.
5. If you develop diarrhea or abdominal pain as a symptom of covid-19, there is a unique probiotic, *Bacillus subtilis* strain B-7092 (Tundrex) that may actually kill the virus, because of its ability to produce alpha-interferon, the natural substance against which the SARS-CoV-2 virus is most vulnerable. This is available at www.tundrex.co (<http://www.tundrex.co>).

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