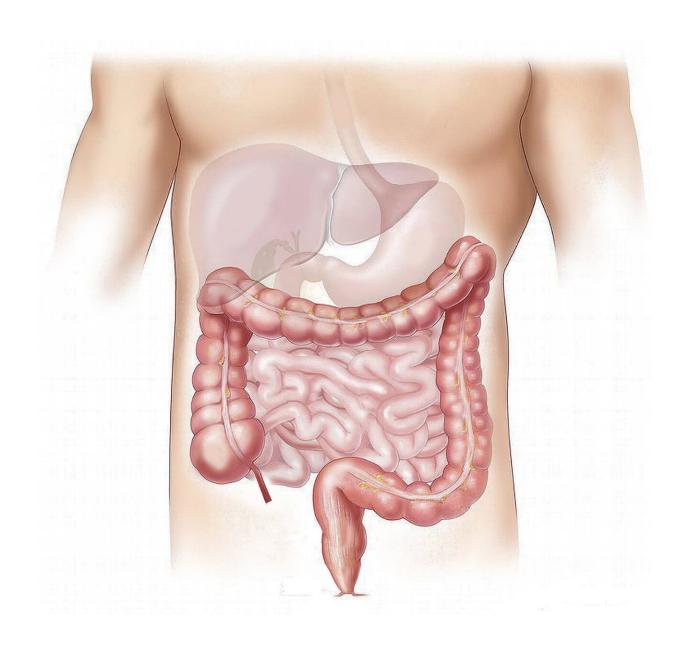


Voyages into the small intestine shed new light on ways to improve gut health

June 17 2024, by Christopher Damman





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Microbiome research to date has been much like the parable of the blind men and the elephant. How much can be said about an elephant by examining just its tail? Researchers have studied what is most readily available—stool rescued from a flush down the toilet—but have been missing the microbial masterminds upstream in the small intestine, until recently.

Likened by some scientists to <u>another human organ</u>, your <u>microbiome</u> is collectively the <u>tens of trillions</u> of microorganisms that live in interconnected populations on and in your body. They serve as miniature sentinels that help <u>protect your body's surfaces</u> from pathogenic invaders. In the upper intestine, distinct microbial populations also aid in <u>digestion</u>, <u>metabolism</u> and even <u>immunity</u>.

I <u>am a gastroenterologist</u> who has spent the past 20 years studying the microbiome's role in health and disease. Advances in technology are helping scientists investigate the <u>small intestine</u> microbiome and the promise it holds for better understanding and treating many diseases.

Big transformations come from small places

Certain members of the small intestine microbiome are linked to <u>obesity</u> and <u>overweight</u>, while other microbial members are linked to a healthy metabolic state. Indeed, small intestine microbes aid in digestion by turning certain <u>simple carbohydrates</u> into the molecular building blocks



of a healthy gut and body.

While analogous in function to the colon, <u>small intestine metabolites</u> can be quite distinct from the fiber-derived <u>metabolites of the large intestine microbiome</u>. Some small intestine metabolites help regulate the upper gut's production of <u>GIP</u>, a sister molecule to the lower gut hormone <u>GLP-1</u>, which makes up the weight loss and type 2 diabetes drugs <u>Wegovy and Ozempic</u>. Together, with another lower gut hormone called <u>PYY</u>, this triumvirate is critical for coordinating your body's response to food by regulating your appetite and blood sugar.

Monjaro is an incrementally more powerful combination of GIP and GLP-1 compared with Wegovy and Ozempic. The full complement of these hormones is naturally stimulated by the breakdown of products from both the large and small intestine microbiome.

The upshot on gut breakdown

Research has linked a disrupted small intestine microbiome to diseases of the gut. These include <u>irritable bowel syndrome (IBS)</u>, <u>small intestinal bacterial overgrowth (SIBO)</u>, <u>Crohn's disease</u> and <u>celiac disease</u>.

These diseases are thought to arise partly from disturbances in the way the microbiome breaks down food. Celiac disease, for example, is associated with the small intestine microbiome's decreased ability to digest gluten. IBS and SIBO are linked to the opposite: the small intestine microbiome's ability to too readily ferment fibers and sugars.

Foods like wheat, garlic, onion, beans and certain processed products that are high-in FODMAPs—a set of fermentable short-chain carbohydrates—have been shown to contribute to symptoms in individuals with SIBO and IBS. Lactose-rich dairy is a high FODMAP food group implicated in lactose-intolerance and linked to an overzealous



small intestine microbiome.

The body's not-so-diplomatic immunity

Diseases associated with the small intestine microbiome aren't limited to metabolism and the gut. In the gut's lining resides a virtual embassy of <u>immune cells</u> that remain in an ever-vigilant state surveying the motley stream of <u>microbial and nutritional antigens</u> passing through your gut.

Compromise in the security systems that separate the fecal stream from the rest of the body and the processes that keep immune responses in check are hypothesized to play a role in triggering various <u>autoimmune conditions</u> in which the body becomes confused as to what is a friend and what is a foe.

Studies have linked inflammatory changes in the small intestine microbiome to <u>type 1 diabetes</u>, where the body's circulating immune cells attack insulin-producing cells in the pancreas, and to the extraintestinal symptoms of <u>celiac disease</u>, where immune cells can lead to destructive processes in the body's eyes, skin and joints.

Lights shed in and on the tunnel

Up until very recently, small intestinal research has moved slowly. Scientists relied on <u>upper endoscopy procedures</u>, which involve sedation and inserting a small camera at the end of pinky-thick tubes through the mouth into the very first part of the small intestine.

One of the few alternatives to endoscopies has been studying patients who have <u>had intestinal surgeries</u> that leave direct portals into their small intestine via a hole in their abdominal wall.



Newly developed technologies are removing the need for sedating medications and unique anatomical situations by allowing scientists to more easily sample the furthest reaches of the gut. Such technologies include <u>camera capsules tethered to angel-hair-thin filaments</u> and other even more <u>streamlined devices</u> that create minimally invasive direct lines of access to the small intestine. Researchers have also developed <u>capsules with sample compartments</u> that open when they reach certain acidity levels in the body.

These new sampling techniques have unlocked unprecedented access to the upper gut, paving the way for new insights and therapies. In a real-life parallel to a childhood favorite, "The Magic School Bus, Inside the Human Body," researchers can now ride along through the gut like Ms. Frizzle and her class, shining light on the microbial secrets held within.

Accrued alliance in a still-crude science

Therapies based on early understandings of the gut microbiome have included approaches ranging from <u>probiotics</u> to <u>fecal transplants</u> and <u>prebiotics</u> to <u>fermented foods</u>.

But new treatments for gut health are still in their early days. Studying the small intestine could provide insights to improve therapeutic development. A couple of promising future possibilities include partnering small intestine bacteria with their preferred prebiotics and personalized combinations of low FODMAP prebiotics designed to avoid small intestine fermentation.

Treatments that <u>partner food and the microbiome</u> are likely early harbingers of what's to come in the rapidly developing field of microbiome medicine. Researching the small intestine—and not only the gut's tail end—might just be microbiome medicine's most pioneering upstream start.



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Provided by The Conversation

Citation: Voyages into the small intestine shed new light on ways to improve gut health (2024, June 17) retrieved 26 June 2024 from https://medicalxpress.com/news/2024-06-voyages-small-intestine-ways-gut.html

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