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# *Digesting the* **Microbiome**


Your weight, mood, skin, dental health, immune system, gut health and more depend on your resident microbial community. Here's how to keep it healthy.







By now, you've gotten the message:

*Keep your resident bacteria healthy  
and your gut will thank you.* 

For more than a decade, health practitioners have prescribed probiotics alongside antibiotics to fend off the gastrointestinal distress that can result when we wipe out our friendly inner-bugs, letting unfriendly ones take hold. Fermented foods and probiotics have become accepted go-tos for general digestive health, with consumers spending \$2.4 billion on probiotic supplements alone in 2018, according to *Nutrition Business Journal*. In extreme cases of *clostridium difficile*, a particularly brutal colon infection, doctors will go so far as to swap “bad” gut bacteria with “good” via a fecal transplant.

But a decade after the National Institutes of Health launched its Human Microbiome Project, kick-starting a global wave of microbiome research, science has revealed that the 100 trillion bacteria residing in and on us impact far more than just our bellies. “Ten years ago, people were saying eat yogurt and you won’t get diarrhea. Today, we know that our microbes also influence our central nervous system, our immune system, our metabolism and many other biological processes,” says Erica Sonnenburg, PhD, a microbiome researcher at Stanford University and co-author of *The Good Gut: Taking control of your weight, your mood and your long-term health* (Penguin Group, 2015).

Research has also illuminated how very different one person’s microbiome—or resident microbial community—is from another’s, spawning a slew of Do it Yourself tests to help people personalize their healthcare. Meanwhile, industry innovators have moved well beyond the yogurt aisle, rolling out patented bacterial-strain-specific ingredients aimed at certain health conditions, and biome-friendly personal care products. “Essentially, we’ve discovered this whole new organ that we didn’t know existed before,” says Lauren Ambrogio, chief operating officer of ABiome Therapeutics, a start-up specializing in microbiome-friendly skin therapies. “If we treat it right and restore it to optimal health we believe we can have a major impact on people’s lives. It’s an exciting time.”





# The forgotten ORGAN

Most people envision their bodies as collections of cells, which make up vital organs. Sonnenburg sees it differently. “We need to think about ourselves as composite organisms made up of human cells and bacterial cells,” she says. “Your microbes are as integrated into your biology as your heart or lung cells are.”

In fact, all together, our collection of microorganisms, “or microbiome,” weighs about the same as our brain (3 to 4 pounds). We have more resident bacteria than human cells, and our bacterial DNA outnumbers our human DNA by as much as 300-fold. Depending on where and how we live, humans host somewhere between 700 and 1,600 different species. Most inhabit the gut, but the mouth, skin, genitals and nasal passages are also teeming. Like individual instruments in an orchestra, each type of bacteria play a unique role in our symphony, keeping various bodily systems healthy or—when things go awry—fueling disease.

## It starts in the belly

By far the most studied aspect of the microbiome is the link between gut flora imbalance, or dysbiosis, and digestive health woes. Taking antibiotics, which can wipe out beneficial bacteria in the bowel, can make way for pathogenic bacteria that causes temporary diarrhea or the more serious and long-term *Clostridium difficile*.


Small intestine bacterial overgrowth (SIBO) occurs when healthy bacteria living in the large intestine grow up into the small intestine, creating bloating, stomach cramps and loose stools. It can eat away at the mucous lining of the intestinal wall, enabling bacteria to seep into our circulation, inflaming our systems and making us sick (a condition sometimes called “leaky gut”).





Our gut bacteria is also in constant communication with the part of the immune system located in the intestine, says Sonnenburg, describing the gut microbiome as a “dial” that controls the sensitivity of the system. If an imbalanced gut cranks that dial up too high, prompting the immune system to have a hair-trigger response to benign exposures, it may contribute to auto-immune disorders like allergies, asthma and arthritis.

Numerous studies have shown that children exposed to a lot of antibiotics have a higher risk of developing allergies and asthma later in life, while those exposed to good bacteria, via food, probiotics or even pets, are at lower risk.

*“The microbiome is the  master switch to our metabolism.”*

### Healthy weight

The healthy-gut-healthy-weight connection is also a strong one. Bacteria in the gut dine on the remnants of carbohydrates we’ve eaten and produce “drug-like” waste products that provide instructions to our physiology. Some push the levers instructing us to burn fat or store fat; others influence whether we are full or hungry.

“The microbiome is the master switch to our metabolism,” says Raphael Kellman, MD, author of *The Microbiome Diet: The scientifically proven way to restore your gut health and achieve permanent weight loss*. (Da Capo Lifelong Books, 2015)

“If there are changes in the percentages of certain bacteria it loses its ability to maintain a healthy weight.” For instance, studies suggest that *Helicobacter pylori* (long maligned as the source of peptic ulcers) can also play a positive role in weight maintenance by regulating the production of the “hunger hormone” ghrelin and the fullness hormone leptin. When doctors wipe it out with antibiotics, “your microbiome has more difficulty shutting off that hunger signal and turning on the fullness signal,” Kellman writes.





Other beneficial bacteria produce short-chain fatty acids such as acetate (an anti-inflammatory) and butyrate (which nurtures the gut lining and improves insulin sensitivity). Research shows obese and overweight people tend to have too much of the bacterial genus *Firmicutes*, and too little *Bacteroidetes*, while in lean people, the ratio is reversed.

And when researchers transplant gut bacteria from an obese person into a lean and healthy mouse, the mouse quickly gains weight, studies show. While research is in its early stage, some clinical trials have shown supplements containing *Lactobacillus rhamnosus* and *Lactobacillus gasseri* may support weight loss and weight maintenance.

## Matters of the brain


Beneficial bacteria have also been linked to improved mental and cognitive health, primarily due to their ability to switch on or off genes that control inflammation (a key culprit behind Alzheimer's, Parkinson's and stress-related disorders like PTSD).

They also produce chemical messengers that communicate with the brain via the vagus nerve, which stretches from the intestines to the brainstem, and influence stress hormones such as cortisol and brain-derived neurotrophic factor, which support brain growth. Gut bacteria themselves also produce neurotransmitters such as dopamine and serotonin.

"Perhaps no other system in the body is more sensitive to changes in gut bacteria than the central nervous system," says David Perlmutter, MD, author of *Brain Maker: the power of gut microbes to heal and protect the brain* (Little, Brown and Company, 2015).

New studies show that children exposed to plenty of beneficial bacteria when they are young (via things such as a vaginal birth, a diet rich in fermented foods or exposure to dust and pets as a child) tend to be more stress resilient in adulthood and may have lower risk of mental illness.

"If you are not exposed to these types of organisms, your immune system doesn't develop a balance between inflammatory and anti-inflammatory forces, and you can develop a chronic, low-grade inflammation and exaggerated immune reactivity that makes you vulnerable to allergy, autoimmune disease and, we propose, psychiatric disorders," explains Chris Lowry, a University of Colorado Boulder researcher.



*"If you are not exposed to these types of organisms, your immune system doesn't develop a balance between inflammatory and anti-inflammatory forces".*

Most research to date has been in animals, but a few small human studies have begun to show promise for what some call “psychobiotics.” One study of 40 patients with depression, published in the *Journal Nutrition* in 2016, found that those who took a combination of *Lactobacillus acidophilus*, *Lactobacillus casei* and *Bifidobacterium bifidum* for eight weeks had significantly decreased depression scores. Another industry-sponsored study, published in the journal *Food and Nutrition*, looked at 40 patients with major depressive disorder. It found that those who took a supplement made with Sabinsa’s *Bacillus coagulans* MTCC 5856 (LactoSpore®) for 90 days not only saw their inflammatory bowel disease symptoms improved, but also saw their depressive symptoms decrease.

## A glowing complexion

The skin hosts its own distinct bacterial community, which plays a key role in protecting it from ultraviolet rays, infection, and skin disorders. Some bacteria are part of the normal, friendly flora on the skin but can cause problems when they become overabundant: For instance, everyone hosts *Propionibacterium*, but in excess it has been linked to acne. Many people host *Staphylococcus*, but too much has been linked to atopic dermatitis or eczema.

Experts contend that in our infatuation with cleanliness, we have washed away and even eradicated some of our friendly skin inhabitants, making way for problems. Today, a host of companies have rolled out microbiome-friendly cosmetics, and a few dermatologists have begun to prioritize microbiome health to support skin health from the inside out. “Taking good care of our gut bugs is the first step to keeping our skin healthy and glowing,” says dermatologist Whitney Bowe, author of *The Beauty of Dirty Skin* (Little, Brown and Company, 2018).

*“Taking good care of our gut bugs is the first step to keeping our skin healthy and glowing.”*





## Healthy mouth

No discussion of the microbiome would be complete without mention of the mouth. “The oral microbiome is much-less studied, but I believe it’s something the dental community should be paying more attention to,” says Steven Lin, an Australian dentist and author of *The Dental Diet* (Hay House Inc., 2018)

Like with the skin and gut, a healthy oral microbiome can serve as a shield against disease. But by overusing things such as anti-microbial mouthwash and fluoride-rich toothpaste, we wipe out those helpers, says Lin, opening the door not only to dental problems such as periodontal disease, but—because mouth microbes often end up in the gut — other health issues.

One 2017 study of 1,206 individuals found that people who used antimicrobial mouthwash twice a day had a 55 percent higher risk of developing diabetes. The theory: Certain microbes in the mouth produce nitric oxide, which regulates insulin levels. Without them, insulin spikes and diabetes risk increases.

Other studies show that dental probiotics can reduce plaque, kill bacteria and play a role in reducing gum disease and bad breath. In addition to steering clear of refined vegetable oils, white flour and sugar (which bad bacteria love to feast on) Lin recommends a probiotic-infused toothpaste free of antimicrobials (charcoal and oil-based varieties are hitting the market) and an alcohol-free mouthwash.





# What makes a HEALTHY MICROBIOME?

**A decade and more than \$150 million after the birth of the microbiome-research field, scientists say they have as many questions as answers. But a few overarching takeaways have emerged:**

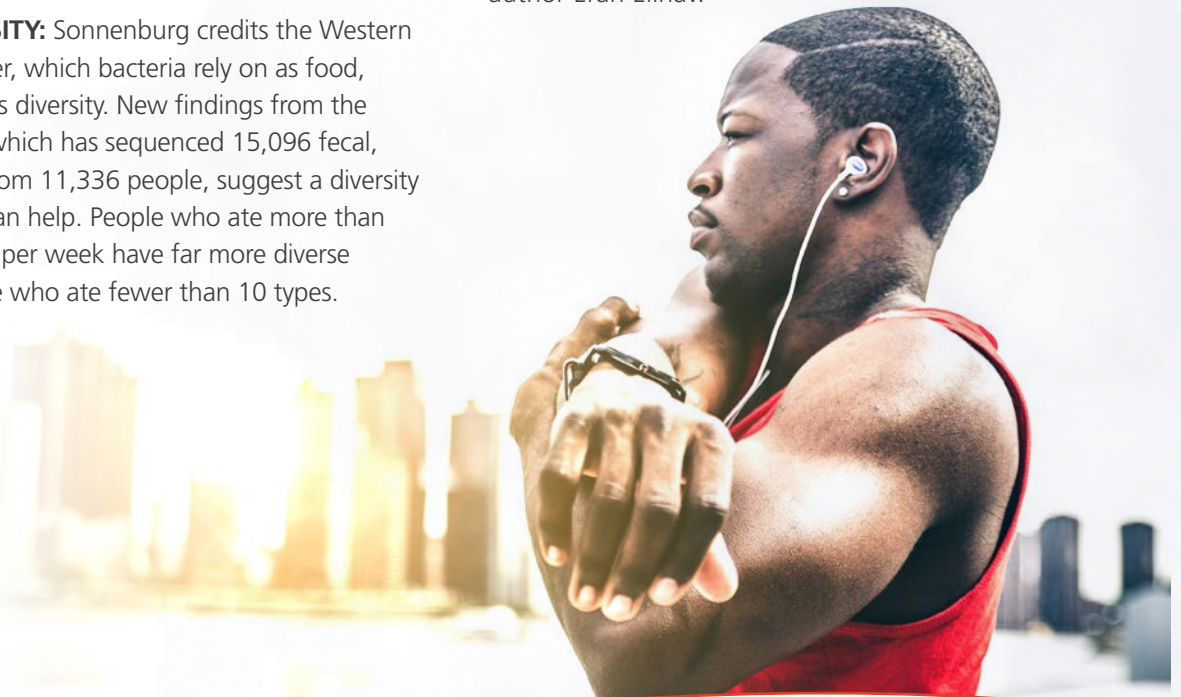
**DIVERSITY MATTERS:** Humans host more than 10,000 different microbial species, according to the Human Microbiome Project, with individuals hosting anywhere from a few hundred to a few thousand at any given time. People with more bacterial diversity tend to be healthier. But in the West, we are losing diversity. In one recent study, scientists looked at stool samples from hunter-gatherers around the world and found they had twice as many species as people from developed countries in the West. They also had species that we no longer host at all. "The question now, is: What did these species do?," says Sonnenburg. "If we had them before and now they are gone, what does that mean for human health?"

**DIET IMPACTS DIVERSITY:** Sonnenburg credits the Western diet's lack of dietary fiber, which bacteria rely on as food, for the decline in species diversity. New findings from the American Gut Project, which has sequenced 15,096 fecal, oral and skin samples from 11,336 people, suggest a diversity of plant consumption can help. People who ate more than 30 different plant types per week have far more diverse microbiomes than those who ate fewer than 10 types.

**THE MICROBIOME FLUCTUATES:** Hunter-gatherer populations show marked fluctuations in their microbiome from season to season, with some bacteria species disappearing during the dry season when they eat more meat and then returning in the wet season when they eat more fruits and vegetables. This suggests that the microbiome can be changed fairly quickly via diet.

**DIFFERENT PEOPLE RESPOND DIFFERENTLY:**

Mounting research suggests that, based on a person's genetic makeup, diet and other factors, individuals respond differently to probiotics. One study of 15 volunteers published in September in the journal *Cell Press* showed that while some people respond well to probiotic supplements, others are unable to colonize them. "This suggests that probiotics should not be universally given as a one-size-fits-all supplement. Instead, they could be tailored to the needs of each individual," said senior author Eran Elinav.







# *A new age of* **PERSONALIZATION**

**With mounting evidence suggesting that what works for one person may not work for another, several companies are rolling out new DIY tests aimed at helping consumers personalize their microbiome-health program.**

**ONEGEVITY:** In 2019, dietary supplement company Thorne will launch a new venture called Onegevity, which will combine genetic tests (via saliva), microbiome analyses (via fecal samples) and ultimately blood tests to provide a more complete assessment of a person's inner-microbial world. "Different people have different gut environments depending on their diet and genetic background so to really personalize a program you need to look at more than just the microbiome," says Bodi Zhang, chief scientific officer at Thorne. For instance, some people may have a genetic variant that prompts their gut microbes to produce excess TMAO — a metabolite that can lead to heart disease — when the host eats red meat. Using machine-learning technologies the company will provide personalized diet and supplement advice to users. The company will also use the data (unless people opt out) to develop new supplements, paying a dividend to those who agree to share their data.

**VIOME:** Launched in 2016, Viome uses "metatranscriptomic" sequencing technologies to provide consumers with information not only about which specific strains of bacteria are living in their gut (based on a fecal sample), but also which metabolites (biologically active waste products) they're producing and what they are doing, and what other enzymes and proteins are present. Then it uses artificial intelligence programs to provide personalized dietary advice via a smart-phone app called Vie. "Food that is good for you may be harmful for me, and food that is good for me today may be harmful for me tomorrow," says Viome CEO Naveen Jain.

**UBIOME:** Since launching its inaugural DIY test in 2012, industry pioneer Ubiome has added two condition-specific tests available only through health practitioners. SmartJane uses vaginal swabs (which women can collect themselves at home) to test for HPV, four other sexually transmitted diseases and imbalances linked to bacterial vaginosis. SmartGut, looks specifically for microorganisms related to irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's Disease. Its direct-to-consumer test, the Explorer, has also been refined, with a time-lapse option offering testing before, during and after a lifestyle change.





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# *Gut feeling:* **WHAT LIES AHEAD FOR THE MICROBIOME?**

In addition to working toward a more personalized approach, industry leaders are exploring the drug-like properties of microbial waste products with an eye toward possible pharmaceutical applications. Others are working to identify and bring back “vanished taxa” or beneficial bacteria that have been driven extinct by Western diets and practices. And some are exploring precisely how our gut bacteria influence other things, like the way we respond to medications.

“I think in the future, physicians will track your microbiota to determine proper dosing for drugs or even use certain probiotics to increase the effectiveness of medications,” says Sonnenburg. “We are headed toward an era of personalized medicine and the uniqueness of our microbiota will be as important as our individual human genome in determining how disease treatment will be tailored to each person.” That said, she also hopes to see a day when, from the moment a child is born, the health of his or her microbiome becomes a priority:

Babies not born vaginally (which naturally inoculates them with good bacteria) would be deliberately exposed to good bacteria. Antibiotic medications and household antiseptics would be avoided if possible. Fermented foods such as yogurt, kimchi and sauerkraut would become a daily mainstay. And everyone would do their best to eat more dietary fiber.



# 5 tips for consumers



**1.** Eat bacteria every day. Yogurt, kimchi, fermented vegetables, kefir and miso are all good options but supplementing is also often necessary.



**2.** Eat more fiber, especially the non-digestible carbohydrates known as prebiotics, which serve as food for your gut bugs. Good sources include carrots, asparagus, leeks, onions and chicory root.



**3.** Look for personal care products that don't contain antibacterial agents.



**4.** Get a pet. Kids who grow up with furry pets, which expose them to more bacteria, grow up to be more stress-resilient and have lower risk of autoimmune disorders.



**5.** Steer clear of antibiotic medications and meats containing antibiotics whenever possible. And be sure to pump up the probiotics when you do need to take antibiotics.

## THE NOT-SO-SECRET INGREDIENT

U.S. consumers are projected to spend about \$2.4 billion on probiotic supplements in 2018, up from \$425 million in 2008, according to *Nutrition Business Journal*. Throw in functional foods and beverages (which constitute about 80 percent of sales) and the global probiotics market is expected to reach \$64 billion by 2022.

## Here's a glance at what's new and what's next in the ingredient space

**STRAIN-SPECIFIC INGREDIENTS:** "Strains do matter with probiotics, and today we have research that identifies which strains seem most effective for what. This has allowed for manufacturers to formulate condition-specific probiotic products," says Shaheen Majeed, president worldwide for ingredient company Sabinsa. For instance, LactoSpore has been found to be effective in the management of Irritable Bowel Syndrome with co-existing depression. Certain strains of *L. rhamnosus* (GR-1) and *L. reuteri* (RC-14), marketed by other ingredient companies and now found in women's health products, have been shown to reduce urinary tract infections. And *L. gasseri* (BNR17) has been shown to aid weight loss.






**SPORE-FORMING PROBIOTICS:** Heat and other manufacturing processes can kill bacteria, and simply sitting on a shelf can be deadly to them, too. To address this, several companies have rolled out “spore-forming” bacteria ingredients, such as Sabinsa’s LactoSpore, which forms protective shells around themselves enabling them to sit dormant for years without losing efficacy. Once they enter the warm, moist environment of the human GI tract, they germinate and become active. Their availability has ushered in a wave of shelf-stable probiotic-infused functional foods, ranging from granola and peanut butter to hot tea, snack puffs and frozen yogurt.

**PREBIOTICS:** Sales of prebiotics — fibrous non-digestible carbohydrates that serve as food for beneficial bacteria — are on the rise, with some analysts pegging them as the next “super-ingredient” for digestive health. In 2018, the first year *Nutrition Business Journal* tracked sales, consumers spent an estimated \$96 million on prebiotic supplements and \$658 million on synbiotic supplements. Look for a slew of new products containing both prebiotics and probiotics, as well as organic and Non-GMO offerings.


**ENZYMES:** Sales of digestive enzymes, often billed as key partners to probiotics when it comes to digestion, are also robust, amounting to \$321 million this year from \$196 million in 2007. Digestive enzymes help the body break down food into more easily digestible bits, with protease breaking down protein, amylase converting starch into sugars the body can absorb and lipase breaking down fats. One recent randomized controlled trial of 40 people with functional dyspepsia — a constellation of symptoms including bloating, nausea, heartburn and early satiety — found that those who took Sabinsa’s DigeZyme® (a multi-enzyme non-animal-sourced complex) for 60 days saw significant symptom improvement.

**Curcuminoids:** One unexpected addition to the microbiome-support arsenal may be curcuminoids, multi-faceted biologically-active ingredients found in turmeric. In one recent study of 14 healthy people, University of California, Davis researchers found that those who took Sabinsa’s patented Curcumin C3 Complex® in combination with BioPerine (a black pepper extract) saw the number of bacterial species in their gut increase by 69 percent over eight weeks. The Curcumin C3 Complex also appeared to have “prebiotic-like effects”, with microbes metabolizing it into beneficial metabolites.

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