Living in a Microbial World

Learning to love your bacteria

By David Schardt

“It’s a whole new world,” says Lita Proctor of the National Institutes of Health. “We’re learning that our bodies are shaped not just by the 23,000 genes in the human genome, but also by the more than 8,000,000 genes in the human microbiome.”

Scientists are discovering that the microbiome—the bacteria, viruses, fungi, and other microorganisms (and their genes) that live on or in us—is far more extensive, and may be far more important for our health, than anyone imagined even a few years ago. Here’s what they’re finding.

“Don’t automatically assume that every microbe you come into contact with is a germ, because the vast majority are not disease-bearing,” says Lita Proctor, program manager for the Human Microbiome Project, which is trying to identify the menagerie of microorganisms that are on and in the human body.

“We have to lose this language of warfare,” adds Julie Segre, a geneticist with the National Human Genome Research Institute. “The bacteria that live on our bodies are not necessarily bad, and we should treat them with more respect.”

Scientists are learning that humans and the human microbiome evolved together, and that some of our bacteria help us survive by doing things that we can’t do ourselves. For example, bacteria on our skin turn some of the oils that skin cells produce into a natural moisturizer, notes Segre.

The largest reservoir of bacteria resides in our intestinal tract, where we host about 100 trillion microbial cells and 1,000 microbial species.

“We’re carrying around about three or four pounds of microbes in our gut,” says Proctor. Among other things, the bacteria inside our lower intestinal tract:

■ digest fiber and other components of food that we can’t digest on our own,

■ synthesize vitamins that we may not be getting enough of from our food,

■ release potentially beneficial chemicals in food, like the isothiocyanate in cooked broccoli that may help prevent cancer,

■ stimulate the immune system, and

■ suppress microorganisms that cause food poisoning or other damage.

DESIGNER BACTERIA

No two people have identical microbiomes.

“People have such tremendous differences in their gut microbiota that two people could be 80 or 90 percent different in the kinds of microbes they have,” says Proctor.

“Evolutionarily, we are meant to attract these bugs because that’s the initial signal to activate our immune system,” she adds.

Babies born by Caesarean section, on the other hand, are colonized by bacteria from skin, which they get from their mothers and others they come into contact with. Because of that, they develop a different community of microorganisms, or microbiota, in their gut.

That could explain why C-section babies may have slightly higher rates of asthma and allergies.

“They’re picking up their first bugs from a source other than what was evolutionarily intended, skin instead of vagina,” says Proctor.

(If you’ve had a C-section. They account for only an estimated 1½ percent of asthma cases and 4 percent of food allergies.)

SHIFTING BUGS

Unlike the human genome, the microbiome isn’t static, says Knight. For example, “there are systematic differences in the gut bacteria in the elderly, especially an increase in organisms that are thought to be opportunistic,” he notes.

“We don’t know whether these changes make the elderly more vulnerable to disease,” he adds, “or whether they’re adjustments that have allowed them to live that long.”

Although the research is still preliminary,
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After Knight and his colleagues put 10 volunteers on either a high- or low-fiber diet for 10 days, their gut bacteria changed. “But the alteration is very small and doesn’t last,” says Knight. “It’s likely that any interventions to modify the microbiota based on diet will have to be for a period of years.”

When 12 obese adults followed low-calorie diets for a year, the proportions of the two main groups of bacteria in their gut microbiota shifted toward a pattern seen in lean people. And the more weight they lost, the greater the change.

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“L
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Many probiotics—so-called “good bacteria”—promise to improve your gut bacteria by repopulating your intestines, by crowding out “bad bacteria,” or by restoring some kind of “balance” to your intestinal flora. That may be an oversimplification.

“We’re looking at trillions of microbial cells already in your intestinal tract,” says Lita Proctor. “If you take a probiotic, whether it’s a pill or a food product, the amount of microbes that you ingest and that survive and end up in your gut is so infinitesimal that you can’t say that they overturn the system or outrun the other microbes.”

Probiotics may work in other ways, though, says Yale expert Martin Floch. They may stimulate the immune system or produce antibacterial compounds that keep a lid on other bacteria.

The trick is identifying which probiotics can fix which problems. A bacterium’s name has three parts: the genus (like Lactobacillus), the species (like acidophilus), and the strain (like LA-5). Strains can differ in what they do even within the same species. And only a small number of strains are backed by decent evidence.

The most dramatic demonstration that our microbiome matters: some physicians are treating nasty Clostridium difficile infections with transplants of gut bacteria (see “Très Difficile”). But our bacteria may also affect our risk of obesity and diabetes.

Obesity

Could the bugs in our intestines be making us fat? After all, lean people appear to have different gut microbiota than people who are obese. Scientists first discovered the difference in laboratory mice and rats that are raised in sterile environments. “These germ-free animals are leaner than animals that are colonized with a complex microbial community, even though they eat more food,” says Peter Turnbaugh of Harvard University’s FAS Center for Systems Biology.

Researchers at Washington University in St. Louis “were the first to demonstrate that the transfer of gut bacteria from conventional to germ-free mice produced a significant increase in body fat, even though the animals didn’t eat any more food than they did before,” notes Turnbaugh.

And when Turnbaugh transplanted gut bacteria from obese to germ-free animals, the germ-free animals gained twice as much body fat than if the transplants came from lean animals. “It didn’t matter whether the conventional animals were obese because of a genetic defect or because they were fed a high-fat, high-sugar ‘Western’ diet,” he notes.

Scientists don’t yet know whether transplanting gut bacteria from lean animals into fat animals will make them less fat.

Why do intestinal bacteria appear to make animals gain weight?

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we can’t digest on our own. They also influence human genes involved in storing fat. And obese mice have more energy-harvesting genes in their gut than lean mice do.6 Researchers have now begun to link gut microbiota to weight in humans:

■ Babies with higher levels of *Bifidobacteria* during their first year of life were less likely to be overweight at age seven than babies with lower levels.7

■ Among 36 overweight adolescents, those who lost at least nine pounds during 10 weeks of diet and exercise started the study with different microbiota than those who lost less than four pounds. By the end, only the microbiota of the group that lost the most weight had changed.8

■ Pregnant women who were overweight or who gained excess weight during their pregnancies had a different gut microbiota than pregnant women who were normal weight or didn’t gain excess weight.9

■ Among 1,255 infants born in the Boston area between 1999 and 2002, those delivered by Caesarean section were twice as likely to be obese at age three as those born vaginally.10 The researchers speculated that the difference in the C-section babies’ gut bacteria may have accounted for their increased weight.

“The bacteria in our gut should be considered one more factor, like diet and physical activity, that affects our energy balance,” says Turnbaugh.

But it’s not clear if changes in the microbiome actually cause obesity.

“One of the problems in studying the association of the microbiome with disease is that microbes are very good at exploiting new habitats,” Proctor explains.

“So when we look at diseased tissue and see associated microbes, for example, we have to ask whether the microbes helped cause the disease or whether they just moved in and exploited a new habitat because something about that tissue changed and became attractive to the microbes.”

Weight gain is even more complicated to study, adds Proctor. “By the time someone is obese, so many other things have changed that obesity is almost the end result of a whole cascade of events. It takes decades to become obese, so we may be looking too far away from the original signal.”

Diabetes

When researchers implant gut bacteria from conventional animals into germ-free ones, the animals not only gain body fat, but they become more insulin resistant.5

(If you’re insulin resistant, blood sugar can’t easily enter your cells. People who are insulin resistant have a higher risk of type 2 diabetes and heart disease.)

“There is suggestive evidence that the gut microbiota is different in people with diabetes,” says the University of Colorado’s Rob Knight.

In a Danish study, for example, men with type 2 diabetes had different gut microbiota than similar men without the disease.11 That led Dutch researchers to test whether gut bacteria transplants could lessen insulin resistance in 18 men who had the metabolic syndrome, which is a sign of insulin resistance. (You have the syndrome if you have three of the following: a large waist, low HDL cholesterol, and elevated blood pressure, blood sugar, or triglycerides—see page 3.) The scientists gave half of the men “fecal transplants” from lean men without the metabolic syndrome (using an enema-like procedure). The other half got transplants of their own stool.

After six weeks, insulin resistance and triglycerides declined in those who got the lean men’s bacteria, but not in those who got their own bacteria back, noted the researchers. (The study is slated for publication later this year.)

“I have been studying diabetes for the past 25 years,” noted French researcher Remy Burcelin told *Nature* magazine this spring, and the idea that diabetes may be related to gut bacteria “is the most important discovery that has been made in my field.”

Proctor’s bottom line: “The fact that the microbiome is dynamic and can change can work to our benefit. Our hope is that we can learn to specifically and preferentially alter the properties of the microbiome to either prevent or minimize the effects of disease.”

10. DOI:10.1136/archdischild-2011-301141.