

SundayReview | OPINION

# There Is No 'Healthy' Microbiome

By ED YONG NOV. 1, 2014

LONDON — IN the late 17th century, the Dutch naturalist Anton van Leeuwenhoek looked at his own dental plaque through a microscope and saw a world of tiny cells “very prettily a-moving.” He could not have predicted that a few centuries later, the trillions of microbes that share our lives — collectively known as the microbiome — would rank among the hottest areas of biology.

These microscopic partners help us by digesting our food, training our immune systems and crowding out other harmful microbes that could cause disease. In return, everything from the food we eat to the medicines we take can shape our microbial communities — with important implications for our health. Studies have found that changes in our microbiome accompany medical problems from obesity to diabetes to colon cancer.

As these correlations have unfurled, so has the hope that we might fix these ailments by shunting our bugs toward healthier states. The gigantic probiotics industry certainly wants you to think that, although there is little evidence that swallowing a few billion yogurt-borne bacteria has more than a small impact on the trillions in our guts. The booming genre of microbiome diet books — self-help manuals for the bacterial self — peddles a similar line, even though our knowledge of microbe-manipulating menus is still in its infancy.

This quest for a healthy microbiome has led some people to take measures that are far more extreme than simply spooning up yogurt. In September, the archaeology writer Jeff Leach used a turkey baster to infuse his guts with the feces of a Hadza tribesman from Tanzania. Doctors have carried out hundreds of fecal transplants, particularly to treat people with unshakable infections of the diarrhea-causing bacterium *Clostridium difficile*. The procedure has been spectacularly successful, far more than conventional antibiotics.

But Mr. Leach did not have *C. difficile*. He experimented on himself because he views the Western microbiome as “a hot microbial mess,” he wrote on his blog. Poor diets, antibiotics and overly sanitized environments have gentrified the Western gut, he wrote, “potentially dragging us closer to ill health.” The Hadza, with their traditional hunter-gatherer lifestyle, carry diverse microbial communities that are presumably closer to a healthier and disappearing ideal. Hence the stunt with the turkey baster. Mr. Leach billed it as “(re)becoming human.”

This reasoning is faulty. It romanticizes our relationships with our microbes, painting them as happy partnerships that were better off in the good old days. It also invokes an increasingly common trope: that there is a “normal” or “healthy” microbiome that one should aim for. There is not. The microbiome is complex, varied, ever changing and context-dependent — qualities that are the enemies of easy categorization.

“Healthy” microbes can easily turn rogue. Those in our guts are undoubtedly helpful, but if they cross the lining of the intestine and enter our bloodstream, they can trigger a debilitating immune response. The same microbes can be beneficial allies or dangerous threats, all for the difference of a few millimeters.

Conversely, “unhealthy” configurations of microbes can be normal, even necessary. Ruth E. Ley at Cornell University and colleagues demonstrated this in dramatic fashion when they found that microbiomes go through a huge

upheaval by the third trimester of pregnancy. They end up looking like the microbiomes of people with metabolic syndrome — a disorder that involves obesity, high blood sugar and a higher risk of diabetes and heart disease. These communities might indicate someone on the verge of chronic disease — or merely motherhood. Packing fat and building up blood sugar makes sense when you are nourishing a growing fetus.

Here is another example. Common medical wisdom says that healthy vaginal microbiomes are dominated by the acid-making *Lactobacillus* group that creates an inhospitable environment for disease-causing microbes. But Larry J. Forney at the University of Idaho and colleagues found that a quarter of women didn't fit this pattern, despite being perfectly healthy. They also showed that their vaginal communities can change dramatically and rapidly, even over a single day, flitting in and out of states that are supposedly conducive to disease, but with neither clear causes nor ill effects.

If you tried to determine a woman's health by analyzing her vaginal microbes, the results would be hard to interpret and might be outdated by the time they arrived.

This befuddling complexity is not confined to the vagina. Earlier this year, Patrick D. Schloss at the University of Michigan analyzed microbes from 18 different body parts on 300 volunteers. They were all healthy, with nary a dental cavity among them. And yet, Dr. Schloss found that their microbes varied greatly, and flipped between different states, for as yet inexplicable reasons.

The dynamic nature of the microbiome partly explains the enthusiasm that surrounds it. If scientists identify changes in the human genome that increase the risk of disease, it is hard to rewrite those genes or to find drugs that target them. But the microbiome could theoretically be altered through probiotics, fecal transplants or other means. It is, as some researchers say, the only "organ" that can be replaced without surgery.

But how can you tell when it needs replacing? A bloom of *C. difficile* is an obvious problem, but most other communities are not so easily classified. The microbiome is a teeming collection of thousands of species, all constantly competing with one another, negotiating with their host, evolving, changing. While your genome is the same as it was last year, your microbiome has shifted since your last meal or sunrise.

We need to start thinking about it as an ecosystem, like a rain forest or grassland, with all the complexities that entails. And just as the gorillas and leopards of African forests differ from the wolves and moose of American ones, so, too, do microbiomes vary around the world.

Take the Hadza. Their microbial roll call is longer than a Western one, with both omissions and additions. They are the only adult humans thus far sequenced who are devoid of Bifidobacteria — a supposedly “healthy” group that accounts for up to 10 percent of the microbes in Western guts. But they do carry unexpectedly high levels of *Treponema*, a group that includes the cause of syphilis.

Is this menagerie worse than a Western one? Better? I suspect the answer is neither. It is simply theirs. It is adapted to the food they eat, the dirt they walk upon, the parasites that plague them. Our lifestyles are very different, and our microbes have probably adapted accordingly. Generations of bacteria can be measured in minutes; our genomes have had little time to adapt to modern life, but our microbiomes have had plenty.

It may be that a Hadza microbiome would work equally well in an American gut, but incompatibilities are also possible. The conquistadors proved as much. As they colonized South America, they brought with them European strains of *Helicobacter pylori*, a stomach bacterium that infrequently causes ulcers and stomach cancer, and these European strains also displaced native American ones. This legacy persists in Colombia, where some communities face a 25-fold higher risk of stomach cancer, most likely

due to mismatches between their ancestral genomes and their *H. pylori* strains.

The microbiome is the sum of our experiences throughout our lives: the genes we inherited, the drugs we took, the food we ate, the hands we shook. It is unlikely to yield one-size-fits-all solutions to modern maladies.

We cling to the desire for simple panaceas that will bestow good health with minimal effort. But biology is rarely that charitable. So we need to learn how tweaking our diets, lifestyles and environments can nudge and shape the ecosystems in our bodies. And we need ways of regularly monitoring a person's microbiome to understand how its members flicker over time, and whether certain communities are more steadfast than others.

Our microbes are truly part of us, and just as we are vast in our variety, so, too, are they. We must embrace this complexity if we hope to benefit from it.

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A version of this op-ed appears in print on November 2, 2014, on page SR4 of the New York edition with the headline: There Is No 'Healthy' Microbiome.

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