

Falk lecture highlights the importance of microbes in chronic disease

By Robin Arnette

A rainforest offers the millions of species that inhabit it a home that provides for their every need. This lush, green landscape maintains its ecological balance, because each organism contributes to the rainforest's stability. But, what happens if you remove one species from that environment? The habitat experiences changes that negatively affect the entire community.

According to infectious disease epidemiologist [Julie Parsonnet, M.D.](http://parsonnet.stanford.edu/), (<http://parsonnet.stanford.edu/>) each person is his or her own rainforest. Getting rid of one microorganism, out of the millions that live in and on us, collectively known as the microbiome, changes how this unique ecology develops. Understanding how the microbiome affects human health represents a new frontier of medicine, and research from Parsonnet and others has helped to uncover the role of bacteria in everything from cancer and diabetes to food allergies and obesity.

Parsonnet discussed her work as the featured speaker March 19 for the 2013 Hans L. Falk Memorial Lecture. Stephanie London, M.D., Dr.P.H., and Walter Rogan, M.D., co-hosted the seminar.

The gut is our second brain

Parsonnet said the microbes that live on us constantly communicate with our cells, but the ones that exist in the human gastrointestinal tract may be responsible for the old adage, you are what you eat. If you like to eat sugary or salty snacks, you will enrich your gut with microbes that want those foods. If you stop eating them, your gut bacteria may send signals to your brain telling you to eat more of what they like.

"You may be saying I want the garden salad, but your microbiome is saying, 'I'll take the cheeseburger and fries,'" Parsonnet remarked.

One of the gut microbes Parsonnet has studied is the stomach bacteria *Helicobacter pylori* (*H. pylori*), which causes inflammation of the stomach, or gastritis, and has long been proven to cause peptic ulcer disease. Parsonnet said a 1993 study showed that people who took antibiotics had no recurrence of peptic ulcer disease, while people who took a placebo or antacid therapy had nearly 100 percent recurrence of the illness.

Physicians had known that stomach cancer arose from areas of inflammation called chronic gastritis. Using an epidemiologic design, Parsonnet demonstrated that *H. pylori* was not only a strong risk factor for stomach cancer, but it also significantly increased the risk for stomach lymphoma. Other researchers proved this association by using anti-*H. pylori* antibiotics to eliminate lymphoma.

Since then the [International Agency for Research on Cancer](http://www.iarc.fr/index.php) (<http://www.iarc.fr/index.php>) has classified *H. pylori* as a type 1 carcinogen, but its listing is complicated. *H. pylori* has been linked to many diseases, including diabetes, yet it appears to prevent esophageal cancers, asthma, and maybe even food allergies.

"*H. pylori* is just one bacterium out of the many thousands of bacterial species that live on the human body," Parsonnet said. "I believe we're going to find that most diseases, if not caused by infections, are amplified by the existence of infections."

You are more microbe than human

Parsonnet said that, according to the Human Microbiome Project, we have 4,000 different microbial species in the gut, 800 in the mouth, 1,300 in supragingival plaque on our teeth, and unknown numbers in parts of the body we once thought were sterile. The total translates into ten times the number of microbial cells as human cells, and 100 times more microbial genes, called the metagenome, than human genes. Astonishingly, that's only counting bacteria.



Parsonnet is a professor of medicine in the Division of Infectious Diseases and Geographic Medicine and the Division of Epidemiology at Stanford University School of Medicine. (Photo courtesy of Steve McCaw)



"Dr. Parsonnet has made landmark contributions to understanding the link between infections and chronic disease," London said. Parsonnet and London were residents together at Massachusetts General Hospital in Boston. (Photo courtesy of Steve McCaw)



NIEHS Scientific Director Darryl Zeldin, M.D., presented Parsonnet with the Hans L. Falk plaque, named in honor of the Institute's first scientific director, who made outstanding contributions to environmental health sciences research. (Photo courtesy of Steve McCaw)

“When we say microbiome, we’re mainly talking about bacteria, but there are viruses, bacteriophages — viruses that live inside bacteria — fungi, and mites,” she said. “They’re the ones steering the ship, and we know virtually nothing about them.”

After a thoroughly engaging seminar, Rogan summed up why Parsonnet was a good choice for this year’s Falk lecture.

“Dr. Parsonnet is a rare combination — clinician, scientist, and educator,” Rogan said. “I saw her give a great talk at a meeting several years ago, and I have been trying to get her for the Falk lecture ever since.”



Falk family members look forward to the lecture every year. From left to right, Rogan, Parsonnet, Zeldin, Gabrielle Falk, Stephen Falk, J.D., Raymond Falk, Ph.D., Michael Falk, Donald Falk, M.D., and London. (Photo courtesy of Steve McCaw)

Infections and the growing problem of obesity

Currently, Parsonnet is studying how early childhood infections affect development, specifically weight gain. The traditional view holds that eating too much, and not burning enough, calories makes people fat, but not all food is absorbed. How little or how much depends on whether a child lives in the developed or developing world. Moving a baby from the developing world to the developed world increases its absorption rates.

Microbiome research in mice has determined that transferring the microbiota from a thin mouse to a fat mouse will make the fat mouse thin and vice versa. This change happens without altering the animal’s diet, and suggests there’s more to the story of obesity in the United States. Parsonnet believes the answer may relate to Americans dealing with fewer infections. Since infections make the body expend a lot of energy, better hygiene and the disappearance of vaccine-preventable diseases may have removed a natural barrier that kept us from being heavier.

“In the 1960s and 70s, people had rheumatic heart disease, tuberculosis, or chronic diarrhea as children. They weren’t as healthy as we are today,” Parsonnet said. “Some of this weight gain may be a healthy thing for us, so we should stop fixating on body types that are dated.”

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