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The next frontier for the microbiome: vaginal fluid transplants that take aim at a common condition

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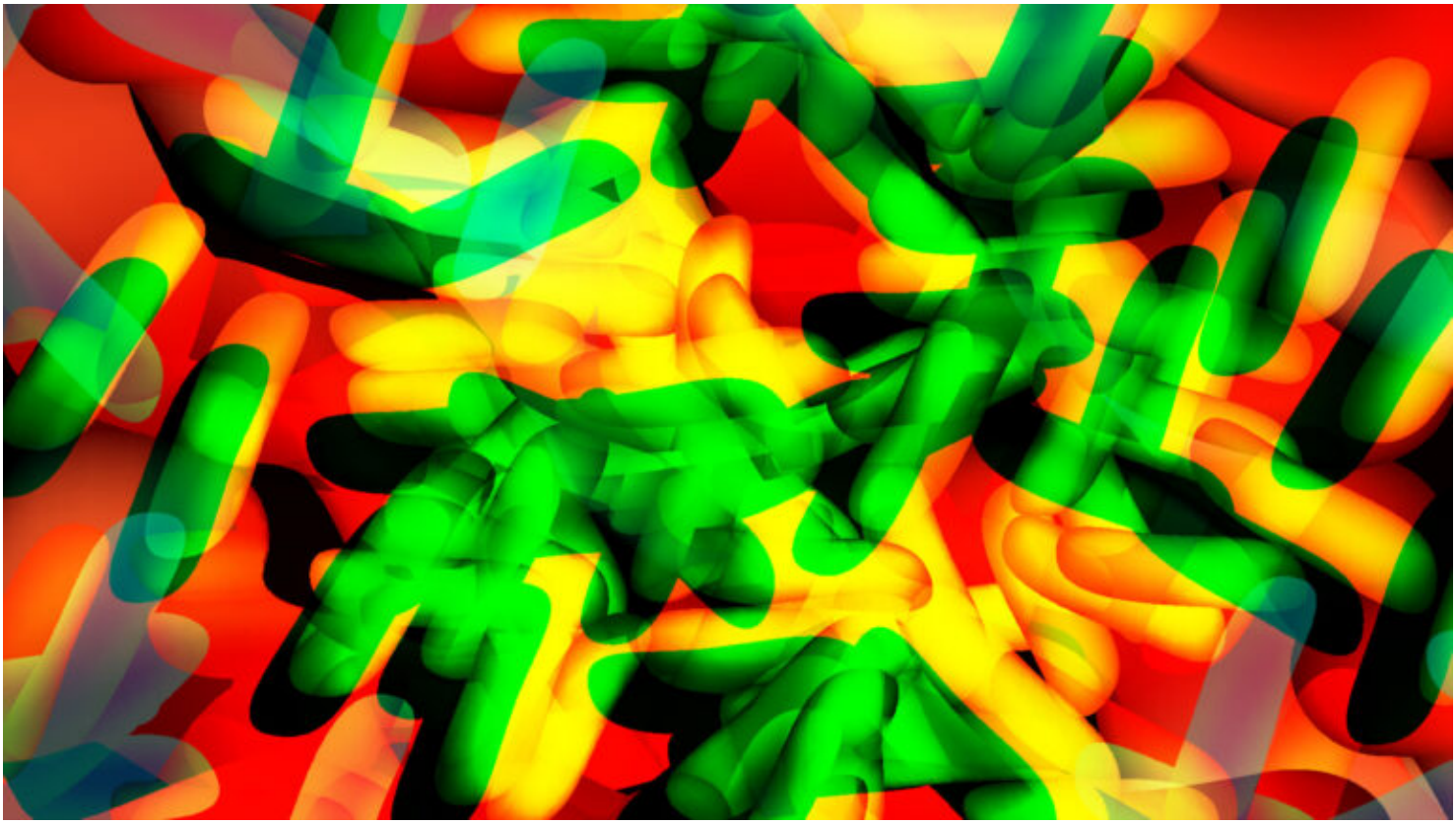
Reprints



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About once a month, bioengineer Laura Ensign-Hodges gets a very personal email from a stranger.

Usually, that stranger will detail her symptoms — an unusual smell and an oddly colored vaginal discharge — and how those symptoms have wrecked her life. She'll tell Ensign-Hodges about the drugs she's tried that haven't worked.

Ensign-Hodges wants to help her and people like her — and soon, she may be able to. She and her colleagues at Johns Hopkins have just received the Food and Drug Administration's approval to begin a clinical trial at a frontier within the emerging field of microbiome science: using vaginal microbiota transplants to treat bacterial vaginosis.

It's one of just two such studies approved in the U.S., both of which were cleared earlier this year. While the potential power of the bacteria living in people's guts has stoked the interest of researchers, patients, and venture capital firms, the vaginal microbiome has, until now, attracted less interest and less funding. In fact, both of the recently approved clinical trials will be looking for research grants.

If one of the treatments succeeds, it could bring long-awaited relief to tens of millions of people — and, perhaps, begin to whittle away at the billions researchers estimate are spent each year on treating the condition's symptoms.

"What we've been doing for the last 40 years is terrible, in regards to improving the vaginal microbiome," said Dr. Craig Cohen, an OB-GYN and reproductive infectious disease specialist at the University of California, San Francisco, who has run clinical trials for Osel, a for-profit company that's separately hoping to develop a microbiome-based drug for the same condition.

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Bacterial vaginosis ought to be an easy target for microbiome-driven treatments; just one type of acid-producing bacteria, known as Lactobacillus, dominates an "optimal" vaginal microbiome.

"In the gut, diversity is the goal. In the genital tract, you want homogeneity," said Cohen.

When Lactobacillus isn't the dominant organism, things often go awry. It's not clear why, though some researchers believe there's a connection between a less acidic environment and the resurgence of other, not-Lactobacillus bacteria.

Whatever the reason, the result could be bacterial vaginosis, the most common vaginal infection, according to the Centers for Disease Control and Prevention. One national survey estimated about 30% of American women between 14 and 49 years old have the condition at any given time; fewer have symptoms. No one is quite sure what causes the condition or what has led to its disproportionate impact on women of color. But the consequences of bacterial vaginosis are clearer.

People with bacterial vaginosis are are a higher risk of contracting HIV or other sexually transmitted infections. The cells of their cervix may be more likely to become cancerous in the presence of a certain virus. Their children are more likely to be born too early or be smaller than they should be.

And the condition can come with damaging psychological effects.

"People are miserable. They feel like they can't have sex, they feel ashamed, they feel dirty," said Dr. Caroline Mitchell, a gynecologist at Massachusetts General Hospital who is running another vaginal microbiota transplant clinical trial for bacterial vaginosis. "It really destroys their quality of living."

Today, the treatment for bacterial vaginosis is antibiotics. At first, those drugs usually bring some relief; in several studies, the vast majority of women found their symptoms were gone within a month after starting treatment.

But more often than not, those symptoms will return. Some researchers in Australia found in 2006 that about half of women who had BV would have it again within a year.

That frustrating statistic makes biological sense. Antibiotics used to treat bacterial vaginosis don't target one bacteria. Instead, the drugs carpet-bomb a

person's microbiome — so while they may make space for Lactobacillus to grow back, they can't directly restore microbial order.

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If bacteria found in vaginal fluid are what people are missing, the solution seems straightforward: just put some back. The reality is more complicated.

Several kinds of Lactobacillus exist, and no one really knows if one strain or species will work better as a treatment than another.

"Because the optimal vaginal microbiome is so simple, it seemed so plausible for so long to just put in the right probiotic Lactobacillus," Mitchell said. "It's not *that* complicated — but it actually is that complicated."

One for-profit company is developing a drug that would only use on strain: L. crispatus, which has been linked in some studies to a decreased risk of preterm birth. The company, Osel, expects to announce the results of a Phase 2b trial by early next year. Unlike the two recently approved trials, Osel's drug wouldn't involve a transplant; instead, it would offer the bacteria as a powder in specified doses through a vaginal applicator.

New DNA sequencing techniques will help scientists untangle the relationships between Lactobacillus strains and other organisms, but those techniques will cost money — as will appropriately screening would-be donors. Testing the blood and vaginal fluid of one donor could cost about $1,000. But neither Mitchell nor Ensign-Hodges currently have the money they need to run their trials. Both are applying for grants from the National Institutes of Health.

Researchers cite a number of different possible reasons why that funding is harder to come by than it has been for other microbiome studies. For one,

women's health issues have a long history of being underfunded and under-researched.

And although both fecal transplants and vaginal microbiota transplants were first done decades ago, vaginal transplants are burdened with an unsavory history. In 1954, Dr. Herman Gardner, a gynecologist at Texas Medical Center and Baylor University's medical school, identified a bacteria he believed was responsible for causing bacterial vaginosis. But Gardner ran one of his experiments by transplanting the vaginal fluid of women who had bacterial vaginosis into healthy people — an obvious violation of ethical norms. That history has clouded later efforts to try transplants, several researchers said.

Another possible reason for the disparity between fecal and vaginal microbiome transplants: the former largely targets a deadly condition. But bacterial vaginosis isn't life-threatening, and the nature of the transplant could mean some doctors and patients are more reticent to try something experimental.

"As gross as poop is, there's a lot of baggage around putting vaginal fluid into someone else's vagina — especially when C. diff is life-threatening, and people don't think of bacterial vaginosis as being life-threatening," Mitchell said.

Still, Mitchell is optimistic that once the trials start, the procedure could find some momentum.

"I've brought it up with a couple of patients in clinic and said, you know, we're working on this," she said. "Granted, the people I see are people who have had this for a very long time. But to a woman, they have said, 'Sign me up.'"

About the Author Reprints

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