

To get to the heart of what causes babies to be born prematurely, David Relman, M.D., Professor of Medicine and of Microbiology and Immunology at Stanford University is studying the bacteria that normally live in harmony inside our bodies. His work has found evidence that a disturbance of the delicate balance of these bacteria may contribute to preterm birth.



It's a mission that has personal resonance for Relman who spent four frantic and exhausting months in the Neonatal Intensive Care Unit (NICU) when his daughter was born three months early. "It was unbelievably stressful," Relman says. His daughter survived and emerged "relatively unscathed" by damage that can come from prematurity, Relman says, but he recognizes that for others, "things don't always go so well." Short-term complications can include breathing problems and an immune system too weak to fight infection. Long-term impact includes a risk of impaired vision and learning disabilities.

"This is not just a problem of being born at the wrong time and surviving the next few weeks," Relman says. "It's really something that potentially has bearing on the rest of that person's life and the people around them."

Relman's research has begun to explain how the bacteria normally present in our bodies can be our allies and partners in health and pregnancy. A balanced mix of bacteria, called microbes, drives a lot of healthy events including nutrition, defense against infections from the outside, and control of hormones.

"We knew almost nothing about this 10 years ago," Relman says. This healthy bacterial mix is now called the "microbiome," or the community of microbes that live on and in the human body.

When something happens to disturb the balance of a person's microbial community in one area of the body, such as the mouth or stomach, that can cause a chain

reaction that upsets the ecology of the body's functions in other areas. Agents as beneficial as antibiotics can wipe out so-called bad bacteria — but at the expense of harming many of the numerically more dominant, good bacteria, with unintended effects. Once the microbial community becomes unbalanced and disorganized, that can provoke or antagonize the body's immune system.

Until recently, a pregnant mother's womb was thought to be a sterile environment that protects her baby from bacteria elsewhere in the body. Relman has found there may be more microbe "invasion" of the mother-baby tissues inside the womb than doctors previously believed.

In the first phase of his work, he is investigating the microbe mix present in pregnant women before and after birth, and the mix in their babies. His overall goal is to find if specific microbes or microbial community patterns are linked to premature birth.

Relman thinks there is strong evidence that microbial communities throughout the body, and especially in a woman's reproductive tract, play a role in maintaining a healthy pregnancy—or in provoking a premature start of labor.

As he explores the significance of this, Relman is taking a "team science" approach made possible by the March of Dimes Prematurity Research Center at Stanford University. He thinks it's smart to collaborate with other kinds of experts to look at prematurity and microbes in new ways.

Working with the other team members of the Center, he can consult with sociologists to look at the microbial community as others would study the behavior of an urban social club. Or he might talk to a climatologist about predicting the health impact of the earth's seasons and weather, to see if that affects fluctuations in microbial communities in pregnant women.

If that sounds wild, that kind of outside-the-box thinking can lead to breakthroughs in understanding problems and finding treatments. "All of us think about problems day to day in different ways, but when we come together, we come up with very interesting ways of viewing this one problem, prematurity, in ways that we wouldn't have otherwise," he says.

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Moms and babies in the U.S. are facing an urgent health crisis:

- In this country 1 in 10 babies is born prematurely each year
- Worldwide 15 million babies are born prematurely each year.
- Premature birth and its complications are the largest contributors to infant death in the United States and globally.
- More than 380,000 babies are born prematurely in the U.S. each year.
- In addition to the human toll, the societal cost of premature birth is more than \$26 billion in the U.S. per year.
- Women of color are up to 50 percent more likely to give birth prematurely and their children can face a 130 percent higher infant death rate.
- In this country black women have maternal death rates over three times higher than women of other ethnicities.
- More than 20 percent of premature babies are born to black women—that's 1 in 5 babies.
- Employers pay 12 times as much in health care costs for premature/ low birthweight babies compared to babies born without these complications.

Because premature birth has many possible causes, each PRC is charged with exploring a different transdisciplinary research target that is likely to be crucial to the prevention of premature birth. Stanford University research themes have unique strengths in the study of the microbiome, the transcriptome, and the immunome. In addition, they also house the Data Repository for all the Prematurity Research Centers enhancing collaboration and data coordination.

"I hope that it takes us to some revelations and insights about causes of prematurity and ways of intervening."

Relman isn't the only one on the team who has a strong personal motivation to prevent preterm births. It turns out that many of his colleagues on the March of Dimes team also have premature babies in their families, and have had to deal with this problem personally as well.

"It feels as though it's a community that's come together out of pieces around a problem for which everyone is willing to dedicate themselves," he says. "The stakes are huge."

THEME 1 LEADERS



David Relman, M.D.

is the Thomas C. and Joan M. Merigan Professor in Medicine, and Microbiology & Immunology, and Co-Director of the Center for International Security and Cooperation



Dan DiGiulio, M.D.

is a Senior Research Scientist and physician in infectious disease.



Susan Holmes, Ph.D.

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Anna Robaczewska

is a Research Assistant, preparing specimens for analysis.

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