

HEALTH | NYT NOW

Study Sees Bigger Role for Placenta in Newborns' Health

By DENISE GRADY MAY 21, 2014

The placenta, once thought sterile, actually harbors a world of bacteria that may influence the course of pregnancy and help shape an infant's health and the bacterial makeup of its gut, a new study has found.

The research is part of a broader scientific effort to explore the microbiome, the trillions of microbes — bacteria, viruses and fungi — that colonize the human body. Those organisms affect digestion, metabolism and an unknown array of biological processes, and may play a role in the development of obesity, diabetes and other illnesses.

During pregnancy, the authors of the new study suspect, the wrong mix of bacteria in the placenta may contribute to premature births. Although the research is preliminary, it may help explain why periodontal disease and urinary infections in pregnant women are linked to an increased risk of premature birth. The findings also suggest a need for more studies on the effects of antibiotics taken during pregnancy.

The new study suggests that babies may acquire an important part of their normal gut bacteria from the placenta. If further research confirms the findings, that may be reassuring news for women who have had cesareans. Some researchers have suggested that babies born by cesarean miss out on helpful bacteria that they would normally be exposed to in the birth canal.

"I think women can be reassured that they have not doomed their infant's microbiome for the rest of its life," said Dr. Kjersti Aagaard, the first author of the new study, published on Wednesday in *Science Translational Medicine*. She added

that studies were needed to determine the influence of cesareans on the microbiome.

Previous studies have looked at bacteria that inhabit the mouth, skin, vagina and intestines. But only recently has attention turned to the placenta, an organ that forms inside the uterus and acts as a life support system for the fetus. It provides oxygen and nutrients, removes wastes and secretes hormones.

“People are intrigued by the role of the placenta,” said Dr. Aagaard, an associate professor of obstetrics and gynecology at the Baylor College of Medicine and Texas Children’s Hospital in Houston. “There’s no other time in life that we acquire a totally new organ. And then we get rid of it.”

She added, “We are just starting to catch a glimmer of this amazing organ that defines placental mammalian biology.”

Dr. Aagaard and her team became curious about the placenta when they noticed something puzzling in earlier research on the vaginal microbiome in pregnant women: The microbes that were most abundant in the mother’s vagina did not match the population in a newborn’s intestine. Scientists had assumed the bacterial profiles would be similar, particularly in babies born vaginally, who were thought to pick up the mother’s bacteria during birth. Dr. Aagaard and her colleagues began to question that assumption.

“It didn’t make a whole lot of sense to us,” she said. “It’s not like babies are hanging out in the vagina. They come shooting out pretty fast.” Also, she said, they emerge covered in a waxy substance called vernix, which most likely helps keep bacteria from latching on.

The researchers wondered if babies might acquire some of their intestinal bacteria before birth, maybe from the placenta.

So they collected placentas in the delivery room from 320 women, mostly black and Hispanic. Most had vaginal deliveries, and some had cesareans. Most of the births were at term, but some were premature.

The scientists searched the placental tissue for bacterial DNA, using a technique called shotgun metagenomic sequencing. They shaved off the outer layer of each placenta and tested samples from the inside, to avoid surface contamination.

“The placenta is not teeming with bacteria, but we can find them, and we can find them without looking too hard,” Dr. Aagaard said.

She said the placenta was less than 10 percent bacteria by mass, comparable to the eye or deeper regions of the skin, but very different from the intestine, which is 90 percent bacteria.

The study provides an “initial snapshot” of the placental microbiome, Dr. Aagaard said. About 300 different types of bacteria turned up, most of them harmless. The team compared the distribution of the types with what had been found previously in other parts of the body, including the mouth, skin, nose, vagina and gut. The closest match by far was between the placenta and the mouth, which, in turn, was much like that in babies’ intestines in the first week of life.

A scientist not involved in the study, Dr. David A. Relman, a microbiome expert at Stanford, said that Dr. Aagaard’s results agreed with those from his lab and others, which had found microbial DNA in amniotic fluid, apparently from the mother’s mouth, gut and vagina.

Dr. Aagaard said she thought that oral bacteria travel through the mother’s bloodstream to the placenta, take up residence there and find their way into the fetus. This is a theory. But research in animals supports it: Oral bacteria injected into a vein in mice home in on the placenta.

The idea also meshes with something that obstetricians have long noted: Women with periodontal disease have a higher risk of having premature or low-birth-weight babies. Treating the disease during pregnancy does not lower the risk. Preventing the disease or treating it before pregnancy seems more important, Dr. Aagaard said.

The study did not provide definitive evidence about periodontal disease because only one participant had it.

A disturbing finding was that when women had urinary infections early in pregnancy, even if the infections were cured, evidence of the bacteria still turned up in the placenta. Those infections increase the risk of premature birth.

The study also found that the microbiome of the placenta in women who had full-term pregnancies differed from that in women who had preterm births. But Dr. Aagaard said the researchers did not know if the difference contributed to the early birth, or was just characteristic of an earlier stage of pregnancy.

Dr. Martin J. Blaser, director of the human microbiome program at NYU Langone Medical Center, and the author of a recently published book, “Missing

Microbes,” said that Dr. Aagaard’s study was important, but preliminary, and that it did not provide information that could be used in treating pregnant women.

“I’m intrigued by the findings about the mouth and also the relationship with preterm labor, which is a really important clinical question,” Dr. Blaser said. “Will this be a productive lead, or will it fizzle out? Time will tell us.”

He said that pregnant women were often given antibiotics, “for all kinds of reasons, many justified, but there’s a slippery slope.” Assuming that the placenta was sterile anyway, he said, doctors thought antibiotics would not affect the fetus. But if the placenta is not sterile, and is instead a portal for bacteria from the mother, he asked, “What are the antibiotics doing?”

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