Medical Xpress

Preemies' gut bacteria may depend more on gestational age than environment

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Barbara Warner, M.D., (left) and nurse Laura Linneman, a clinical research coordinator, check on Skylar Angel in the neonatal intensive care unit at St. Louis Children's Hospital. Skylar and her twin, Bayley, were born prematurely. Warner is co-first author of a Washington University School of Medicine study reporting that the population of bacteria in the intestinal tracts of premature infants may depend more on the babies' biological makeup and gestational age at birth than on environmental factors. Credit: E. Holland Durando/Washington University

Scientists believe babies are born with digestive systems containing few or no bacteria. Their guts then quickly become colonized by microbes—good and bad—as they nurse or take bottles, receive medication and even as they are passed from one adoring relative to another.

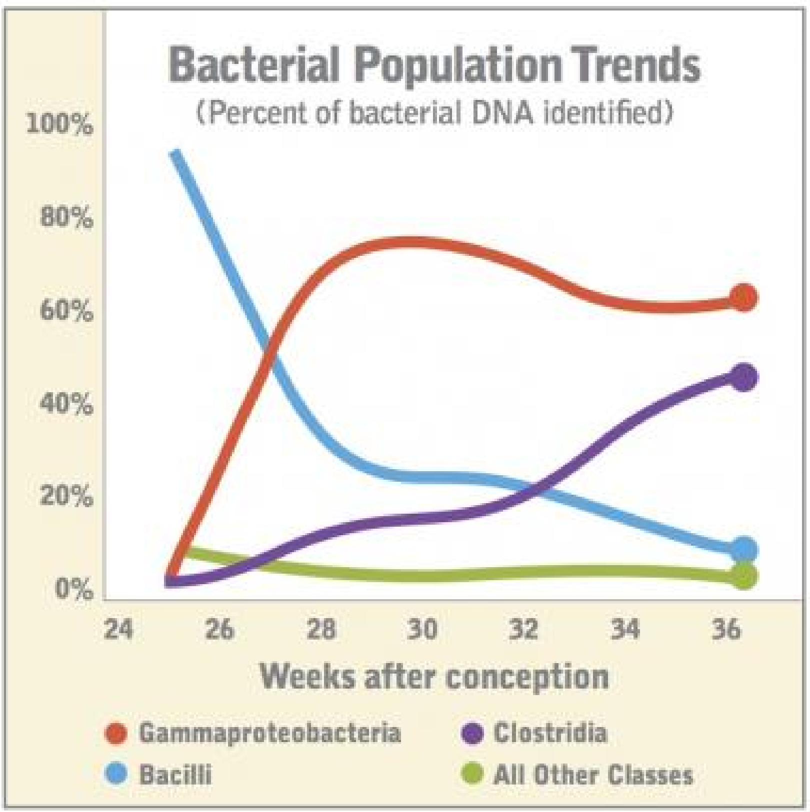
However, in infants born prematurely, researchers at Washington University School of Medicine in St. Louis have found that the population of bacteria in babies' gastrointestinal tracts may depend more on their biological makeup and gestational age at birth than on environmental factors. The scientists discovered that bacterial communities assemble in an orderly, choreographed progression, with the pace of that assembly slowest in infants born most prematurely.

"Your earliest gut microbes probably have lifelong consequences, but we know very little about how these microbial communities assemble," said senior author Phillip I. Tarr, MD, the Melvin E. Carnahan Professor of Pediatrics. "Do these populations form as a result of random encounters, with an infant's gut supporting the growth of bacteria that enter this organ by chance? Or does the host have a role in selecting the microbes? Our research indicates that the gut is destined to define the bacteria that inhabit it. At 33-36 weeks after conception, preterm infants have very similar microbial populations in their guts."

The research appears Aug. 11 in the *Proceedings of the National Academy of Sciences* (*PNAS*) online early edition.

Bacterial colonization has lasting effects—influencing health and development, immune function, resistance to infection, and predisposition to inflammatory and metabolic disorders—yet, until now, little has been known about how the microbes get there.

Collaborators at The Genome Institute at Washington University School of Medicine used DNA sequencing to tally the bacterial populations in 922 stool samples from 58 premature infants. The babies, patients in the neonatal intensive care unit (NICU) at St. Louis Children's Hospital, ranged from 23-33 weeks in gestational age and weighed 1,500 grams (3 pounds, 5 ounces) or less.



School of Medicine researchers found that differing ratios of three major classes of bacteria -- Bacilli, Gammaproteobacteria and Clostridia -- colonized the guts of premature infants in sequence. Credit: Washington University

The investigators found that differing ratios of three major classes of bacteria colonized the preemies' guts in sequence. Earliest in life, a group of bacteria called Bacilli dominated. Then, a class known as Gammaproteobacteria became abundant. Third, the class identified as Clostridia flourished. Environmental factors—including whether the babies' deliveries were vaginal or cesarean, whether they had been given antibiotics, their ages when stools were sampled, and their diets—influenced the pace, but not the order, of the progression.

The researchers noted abrupt changes in each gut's bacterial composition along the way to 36 weeks in gestational age but found that somehow the gut ecosystems adjusted and returned to what seemed to be a preordained progression of bacterial colonization.

"Sometimes the abrupt changes were in the same direction as the overall progression, and at other times they weren't," said Tarr, who is also director of the Division of Pediatric Gastroenterology and Nutrition. "That was unpredictable. But eventually the population proportions would correct, and those three classes of bacteria would remain the major components."

Armed with the knowledge of what occurs in the digestive systems of preemies in a controlled environment, the researchers' next aim to discern what happens in the systems of preemies who don't fare as well, particularly those suffering from necrotizing enterocolitis (NEC).

NEC is a devastating disorder in premature infants that causes tissue death in the lining of the intestinal wall. The syndrome occurs in up to 10 percent of premature infants and is fatal 25 to 35 percent of the time. Scientists believe gut microbes play a part in the disease.

"Research has not made an impact in either prevention or treatment of NEC," said co-first author Barbara Warner, MD, a professor of pediatrics who treats patients at St. Louis Children's Hospital. "The Holy Grail is prevention, and if so much of what happens in the gut depends on the host, this research may help us identify just what increases an infant's risk for developing NEC and help us target therapies."

Warner said she and her colleagues don't yet know the significance of the three bacterial classes that dominated the preemies' gut microbiota. But of the three, she said, Gammaproteobacteria are most intriguing because they are linked to inflammation and because there were so many of these microbes in the infants' guts.

In a healthy, older child's gut, Gammaproteobacteria typically are less than 1 percent of the bacteria. In this study, however, well over 50 percent of the bacteria in many of the premature infants' guts were Gammaproteobacteria. And in some infants, this group of microbes accounted for more than 80 percent of the bacteria.

What that means for preterm infants and how it might affect them in the long term are among questions raised by the new research, Warner and Tarr said.

"This is the largest and most intense sampling of newborn infant guts ever performed using modern sequencing technology, and we believe that the data from this study will be immensely helpful in understanding the human gut," Tarr said. "It is our first glimpse of how these earliest in life bacterial colonizations—events that may have lifelong consequences—occur."

More information: "Patterned progression of bacterial populations in the premature infant gut," by Patricio S. LaRosa et al.*PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1409497111

Provided by Washington University School of Medicine

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