Changed gut bug mix linked to C-section, antibiotics, formula lasts through baby's first year

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Credit: Anna Langova/public domain

Birth by C-section, exposure to antibiotics and formula feeding slow the development and decrease the diversity of a baby's microbes through the first year of life. That is the finding of a study led by researchers from NYU Langone Medical Center and published June 15 in the journal *Science Translational Medicine*.

The study results center on the microbiome, the mix of bacterial species that live on human skin and in our guts, and that co-evolved with humans to play roles in digestion, metabolism and immunity. As rates of children's exposure to C-sections, antibiotic use, and formula feeding have increased in recent decades, the incidence of asthma, autoimmune diseases and obesity has more than doubled. Many studies have now linked these trends, but only a few experiments in mice have shown microbial differences to directly increase disease risk.

"Our results provide evidence that modern practices change a baby's microbial communities in ways that last through the first year," says Martin Blaser, MD, the Muriel G. and George W. Singer Professor of Translational Medicine at NYU School of Medicine, and the study's senior author. "The big, remaining question is whether or not changes in this timeframe, even if resolved later on, affect the founding of microbiomes with lifetime consequences for a child's immune function and metabolism."

"The reasons for links seen between microbial changes and many diseases remain unclear, but our study supports the concept of altered microbiota assembly as a plausible explanation," adds Blaser, also professor of Microbiology at NYU Langone.

In the new study, researchers assessed the effects of modern practices on intestinal microbiota development in 43 New York children, and found multiple changes in the gut microbiomes of the babies based on delivery mode, exposure to antibiotics, and feeding method over. More than 1,000 stool samples were collected monthly from these infants, 24 of whom were born by vaginal delivery and 19 by C-section.

The team then used genomic and statistical techniques to analyze the millions of pieces of bacterial DNA in the samples. Past studies had already matched key DNA sequences to known bacterial species, enabling the team to define each baby's microbiome, and to watch the effect of each practice at intervals over the first two years of life.

The study results reflect concepts in ecology such as diversity and dominance of species. The different ways in which babies acquired their original microbiomes, combined with the factors that changed species balance, were found to determine not only bacterial profile, but also which species came to dominate and when.

Unexpectedly, the study authors found that, compared to vaginally born infants, those delivered by C-section showed significantly greater species diversity in the weeks after birth. However, these measures declined in cesarean-born infants during their first month, after which they displayed lower diversity up to two years of age. The change in birth mode interrupted the natural interplay between diversity and dominance, says Blaser.

The research team also found that antibiotic treatment significantly diminished diversity of bacterial species immediately following birth. Diversity then recovered during the first year of life to resemble that of infants not exposed to antibiotics. Species diversity was decreased in formula-fed children as well during the second year of life.

Beyond the analysis of microbial diversity, the research team also compared each child's set of microbes to an index of species shown to track with normal microbiome development over time. Studies in recent years found a standard pattern of turnover (succession) in children's microbiomes as they age, with species better adapted for the womb giving way to those associated with a diet of solid food.

Using this model, the research team found that microbiota maturation stagnated in C-section delivered infants between six months and two years of age. Similarly, children exposed to antibiotics showed delayed microbiota maturation compared to those not exposed, as did children fed by formula instead of breast milk, but during the second year of life. In total, each of these practices affected the maturation and succession of the microbiota.

As for potential solutions, a pilot study led by co-author Maria Gloria Dominguez Bello, PhD, published in *Nature Medicine* in February found that swabbing babies born by C-section with their mother's birth fluid partially restored the mix of bacteria that coat a newborn's body when delivered vaginally. Larger studies are planned moving forward.

Along with Blaser and Dominguez Bello, all of the study authors were from NYU Langone, including principal author and post-doctoral fellow Nicholas Bokulich, as well as Jennifer Chung, Thomas Battaglia, Nora Henderson, Melanie Jay, Huilin Li, Arnon Lieber, Fen Wu, Guillermo Perez-Perez, Yu Chen, William Schweizer, Xuhui Zheng, and Monica Contreras. The scientists were in the departments of Medicine, Population Health and its Division of Biostatistics, Microbiology, and Obstetrics and Gynecology.

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Of note, a second study published in the same edition of *Science Translational Medicine*, and led by the Broad Institute of MIT and Harvard, found that C-section and antibiotic use had similar effects on the gut microbiomes of 39 Finnish children.

More information: "Antibiotics, birth mode, and diet shape microbiome maturation during early life," *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aad7121

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