Medical Xpress

Study reveals impact of antibiotic treatment, other factors on the infant gut microbiome

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A comprehensive analysis of changes in the intestinal microbial population during the first three years of life has revealed some of the impacts of factors such as mode of birth - vaginal versus cesarean

section - and antibiotic exposure, including the effects of multiple antibiotic treatments. In the June 15 issue of *Science Translational Medicine*, the team led by investigators from Massachusetts General Hospital (MGH) and the Broad Institute describes findings that may help understand how the gut microbiome is established and how the combination of microbes in individual children may contribute to the risk of developing conditions like type 1 diabetes and inflammatory bowel disease.

"One of the key motivations of microbiome research is that the microbial population of early childhood appears to be critical to human health, in that decreased diversity of the gut microbiome has been implicated in a number of allergic and autoimmune diseases," says Ramnik Xavier, MD, PhD, chief of the MGH Gastrointestinal Unit and an institute member at the Broad. "Not only did our study analyze the gut microbiome at a high resolution that allowed us to identify both microbial species and strains, but by following our study participants over time we also were able to uncover findings that would not have been revealed by single samples from each patient.

In collaboration with a team of Finnish researchers they have worked with for several years, the MGH/Broad team enrolled a group of 39 children from whom monthly stool samples were taken beginning after birth and continuing until age 36 months. Each sample was analyzed with a standard, RNA-based sequencing procedure used to identify microbial populations, and more detailed whole-genome sequencing was conducted on about 25 percent of samples to reveal the specific strains of identified microbial species. During the study period, 20 of the participants received antibiotics to treat respiratory or ear infections, with those children receiving from 9 to 15 treatments.

Many features of the developing gut microbiome were found to be consistent across all study participants, with the presence and abundance

of particular species rising and falling at similar age points. The researchers also found several clear differences from the findings of previous studies regarding the impact of breastfeeding. Earlier studies comparing breast-fed with formula-fed children have reported increased abundance of Bifidobacterium species in those who were breast-fed for longer periods of time. All of the children in this study were breastfed for some period of time, and while there was some correlation between the length of breastfeeding and levels of Bifidobacteria, some of the children in this group had low levels of those bacteria even while being breastfed.

Previous studies also have reported finding a particular microbiome signature, with low abundance of the Bacteriodes genus, in cesarean-section-delivered children during the first 6 months of life. In the current study, the researchers found the same pattern in the four cesarean children but were surprised to find it also occurred in seven of the vaginally born children. No identified factors, including maternal antibiotic treatment, differentiated between vaginally born children with or without the low-Bacteriodes signature, but since this pattern has been associated with reduced overall diversity of the microbiome, it bears further investigation, Xavier notes.

Children who had been exposed to antibiotic treatment had a reduction in the diversity of their microbial population, a difference that was even greater in those who also had the low-Bacteriodes signature. Whole-gene sequencing also found that, in antibiotic-exposed children, bacterial species tended to be fewer and dominated by a single strain, instead of the several species and strains seen in those not treated with antibiotics. The analysis of many samples taken over time revealed that the microbiomes of antibiotic-exposed children were less stable, particularly around the time of antibiotic treatment.

The presence of genes known to confer antibiotic resistance rose rapidly

during antibiotic treatment. Levels of resistance genes encoded on microbial chromosomes dropped quickly after treatment was discontinued. But resistance genes encoded on small DNA molecules called mobile elements - one means by which resistance genes can be transmitted among bacteria - persisted much longer after antibiotic withdrawal.

"Some of the things we'd like to investigate next are how the microbiome gets established during the first week of life - particularly what the primary mechanisms of transmission are - how the composition of the early-life gut microbiome affects children's health, and what factors underlie the resilience of the infant microbiome, says Xavier, who is the Isselbacher Professor of Medicine in Gastroenterology at Harvard Medical School and a member of the MGH Center for Computational and Integrative Biology (CCIB). "The kind of high-resolution sequencing done in this study should lead to better understanding of the natural history of the infant gut microbiome and the impact of perturbations caused by antibiotics and environmental factors."

More information: "Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability," *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aad0917

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