Researchers devise methods to identify transmission of microbes from mothers to infants

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It has been assumed that mothers pass on gut microbes to their infants during and just after delivery, a process called vertical transmission, but because of limits in available technology, the evidence of this occurrence has been limited. Now, researchers in Italy have combined laboratory and novel computational techniques to systematically track the vertical

transmission of microbes in a pilot study.

Their results, published this week in *mSystems*, an open access journal from the American Society for Microbiology, found several identical bacterial strains in the microbial communities (the microbiomes) of both infants and their mothers that were distinct from those found in other infants or mothers, a sign of vertical transmission. In addition, transmitted strains from the Bacteroides and Bifidobacterium species were found to be active in both the mother and infant gut microbial communities.

"Early infant exposure is important in the acquisition and ultimate development of a healthy microbiome," said senior study author Nicola Segata, PhD, an assistant professor at the Centre for Integrative Biology at the University of Trento, Italy. "We developed methods to identify the vertical flow of microorganisms from mothers to infants and showed that mothers are sources of microbes that might be important in the development of the infant gut microbiome."

Previous cultivation-free studies have observed the same microbial species within mothers and infants and therefore assumed that transmission occurred "but in reality, unless you can see the same strain or genetic variant, it's very hard to conclude that," said study co-senior author Adrian Tett, PhD, a senior research associate with the Centre. Although some microorganisms have been followed from mothers to infants using time-consuming cultivation approaches, "We demonstrated that vertical transmission can be inferred without using cultivation and will follow up on a larger scale."

There has been debate among scientists whether microbes colonize in the infant gut at birth or in the womb, Segata said. If strong evidence is found that the mother before or during childbirth is likely to transmit a particular microbe that can be detrimental to the infant's future health,

he said, it could be possible to test the mother while she is pregnant and offer some preventative treatment. For example, current practice tests pregnant women for Group B Streptococcus that can cause infection in the infant; if the woman tests positive, drugs are administered just before delivery to prevent transmission of the microbe to the infant.

Segata and colleagues collected fecal and breast milk samples from five mother-infant pairs recruited by a local hospital when the infants were three months old. They collected additional samples from two of the mother-infant pairs again when the infants were 10 months old, and from another mother-infant pair when the baby was 16 months old. They applied a laboratory technique called shotgun metagenomic sequencing to 24 microbiome samples (eight mother fecal samples, eight infant fecal samples and eight breast milk samples) to see which microbes were present. They used an additional tool called metatranscriptomics in fecal samples from two of the pairs to see which microbes were active.

Initially, as expected, the mothers' intestines had greater microbial diversity than those of the infants. However, the gut microbiome of the 16-month-old child had shifted toward a more mother-like composition with an increase in microbial diversity. Breast milk samples had limited diversity shortly after birth; skin microbes were observed in only low numbers in the infants' gut microbiomes, suggesting that skin microbes do not colonize the human gut.

To analyze microbial transmission from mother to infant, the team further analyzed the metagenomic samples at a finer level to assess specific bacterial strains using newly developed computational approaches. One infant harbored a strain of the common infant bacterium Bifidobacterium bifidum that was 99.96% identical to his mother's but clearly distinct from B. bifidum strains seen in the other infants and mothers, offering strong evidence for vertical microbial transmission. Another infant had strains of two other bacteria,

Coprococcus comes and Ruminococcus bromii, that were over 99% identical to his mother's. From metatranscriptomics, researchers observed some of the same strains of bacteria active in both the mothers' and the infants' guts.

While the results are still early, Segata said, "there is probably a substantial fraction of bacteria in the infant that come from the mothers." In ongoing work, the investigators are studying more mother-infant pairs from the time of the babies' births to over one year of age, including analyses of the mothers' and infants' microbiomes from several body locations. They will compare microbe transmission routes during vaginal and Cesarean section deliveries, breastfeeding, and skin-to-skin contact shortly after birth.

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