Study shows breast milk contains unique set of antibodies

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Breast milk from each individual contains a unique assemblage of antibodies that are surprisingly stable throughout lactation and across pregnancies, according to a new *Journal of Experimental Medicine* study from the University of Pittsburgh School of Medicine.

As a baby's early immunity is directed by antibodies from breast milk, the new research provides insight into why protection against different infections varies among infants and why some develop a life-threatening gut disease called necrotizing enterocolitis (NEC).

"While each milk donor in our study had very different antibody profiles from one another, we found that antibodies from the same donor were quite similar over time—even across the span of months," said senior author Timothy Hand, Ph.D., associate professor of pediatrics and immunology at Pitt's School of Medicine and UPMC Children's Hospital of Pittsburgh.

"This means that if a baby's parent happens to lack particular antibodies—such as those that fend off NEC, they're never going to receive that immunity. This could help explain why some babies get NEC and others don't."

According to Hand, NEC is a devastating inflammatory gut disease that mainly affects preterm infants. NEC, which has been linked with a family of bacteria called Enterobacteriaceae, is about two to four times more frequent in formula-fed babies than those fed breast milk.

Before their immune system matures, babies are protected from harmful bacteria by antibodies transferred via the mother's placenta and through breast milk. These antibodies bind to bacteria in the intestine, preventing them from invading the host.

In an earlier study, Hand and his team found that Enterobacteriaceae in fecal samples of healthy babies were mostly bound by maternal antibodies. In contrast, infants who went on to develop NEC had more bacteria that escaped being bound. Hand suspected that variation in babies' immunity to NEC was because different mothers passed along different antibodies, and the new study lends support to this idea.

Hand and his team analyzed donor breast milk from the Human Milk Science Institute and Biobank in Pittsburgh and Mommy's Milk Human Milk Research Biorepository in San Diego. Using an array of different bacteria, they measured which strains each donor's antibodies bound to.

"Individual donors antibody profiles looked completely different, which is what we had expected but were able to show for the first time," said Hand.

"During pregnancy, B cells travel from the intestine to the mammary gland, where they start making antibodies. The mom is trying to protect her infant using antibodies that she uses to protect her own intestine. Different women have led different lives, have different microbiomes and have encountered different infections, so it makes perfect sense that breast milk antibodies would reflect that variability."

Throughout the breastfeeding period, a mother's milk changes from highly concentrated protein-rich colostrum into mature milk. To learn whether antibody composition changes, too, Hand and his team compared breast milk from the same donors over time. They also looked at the same donors over multiple pregnancies.

"Not only were antibodies similar in donors across one pregnancy, they were also remarkably stable between infants," said Hand. "This suggests that when B cells arrive in the breast tissue, they don't leave. This is important for understanding how babies acquire immunity and how they deal with infections."

The researchers also asked whether breast milk antibodies were different if a donor delivered preterm.

"Some B cells move to the mammary gland during the third trimester, so we wondered if a person delivers before this trimester is complete, would their milk have fewer antibodies," said Hand. "The good news was that we found no difference: Individuals who deliver preterm have just as many antibodies and the same diversity as those who deliver full-term."

Other studies indicate that mother's own milk is the best food for reducing a premature baby's likelihood of developing NEC, but if that isn't available, donor milk is an important substitute or supplement. This milk is sterilized to kill bacteria, but whether this process also affects antibodies had not been tested.

Hand and his team found that pasteurization reduced antibody levels in donor milk. While this likely means that infants fed donor milk receive fewer antibodies than those who get milk directly from their mother, Hand said that more research is needed to understand what levels of antibodies are protective against diseases like NEC.

In the future, better understanding of specific bacteria that are most dangerous for preterm infants at risk of NEC could help researchers develop antibodies that could be added to formula or breast milk to boost immunity.

More information: Chelseá Johnson-Hence et al, Stability and heterogeneity in the anti-microbiota reactivity of human milk-derived Immunoglobulin A, *Journal of Experimental Medicine* (2023). DOI: 10.1084/jem.20220839. rupress.org/jem/article-lookup … 10.1084/jem.20220839