Milk boost: Research shows how breastfeeding offers immune benefits

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When infants breastfeed, they receive an immune boost that helps them fight off infectious diseases, according to recent research from Binghamton University Associate Professor of Anthropology Katherine Wander.

She is the lead author of "Tradeoffs in milk immunity affect infant infectious disease risk," published this June in *Evolution, Medicine, and Public Health*. Co-authors include Masako Fujita from Michigan State University's Anthropology Department, Siobhan Mattison from the University of New Mexico's Anthropology Department and the National Science Foundation; and Frida Mowo, Ireen Kiwelu and Blandina Mmbaga in Tanzania, whose associations include the Kilimanjaro Christian Medical Center and the Kilimanjaro Clinical Research Institute. Binghamton University graduate students were also part of the research team, with tasks ranging from data collection in Tanzania to data-cleaning and analysis. They include Margaret Duris, Megan Gauck, Tessa Hopt, Katherine Lacy, Angela Foligno, Rebecca Ulloa and Connor Dodge.

For the project, the research team studied almost 100 mother and baby pairs in rural Kilimanjaro. Prolonged breastfeeding is the norm in this population and infectious diseases during infancy are very common, even compared to other areas of East Africa. This makes Kilimanjaro an ideal setting to begin to understand how immune protection from milk might affect infectious disease risk, Wander said.

"You most often hear about the immune system of milk in terms of transferring maternal antibodies to infants via milk—which is probably very important—but it seems there's much more going on as well. The immune system of milk is a whole system, capable of mounting immune responses," Wander said. "We're only beginning to understand the full extent and role of the immune system of milk."

Milk and immunity

Mother's milk contains everything needed to mount immune responses, from antibodies to multiple types of immune cells and more. While they originate from the mother's immune system, these components of milk appear to be curated rather than selected at random from the mother's blood, although that mechanism remains poorly understood, Wander explained.

To test the impact of milk's immune system on infant health, the researchers combined a few milliliters of milk with a small amount of bacteria, then placed the mixture in an incubator overnight. They then measured the increase of interleukin-6, an immune cell communication molecule that promotes inflammation. This in-vitro response gives an indication of how the milk's immune system is likely to respond to bacteria encountered in the infant's body—the gut, for example.

The research team also followed the Tanzanian infants to assess whether those who received milk that mounted stronger immune responses during the in-vitro tests were at lower risk for infectious diseases. That appeared to be the case: infants whose mothers' milk mounted larger responses to Salmonella had fewer infectious diseases, particularly respiratory infections such as pneumonia.

But milk that mounted larger responses to Salmonella also tended to mount stronger responses to a benign strain of E. coli, which is common in the human intestinal tract, and these responses weren't beneficial to infants. Infants who received milk that mounted stronger responses to E. coli were at higher risk for gastrointestinal infections. This may indicate that inappropriate responses by milk's immune system—for example, to bacteria normally present in the gut—can be disruptive. Gut bacteria play an important role in preventing diarrhea and other infectious disease, the authors note.

While all immune responses have tradeoffs, the downside of milk—both immediate and common—was a surprising discovery.

"With so much at stake, we really expected the immune system of milk to be very finely tuned to protecting infants against infection," Wander said.

Researchers expected to see, at most, negative effects of inappropriate immune responses somewhere down the line, such as in slower growth or less than ideal microbial flora. But differentiating between microbial friend or foe is a tricky business even for adults' mature immune systems, as is eliminating an infection without damaging the person's own tissues. So, the authors say, maybe they shouldn't have been surprised to see these tradeoffs play out in infants, as well.

In addition to reducing risk for respiratory infectious, milk immune responses may help "train" the infant's developing immune system to respond to dangerous bacteria. More research is needed to determine how immune development calibrates to input, such as experience with infectious diseases, microbial flora and the immune system within milk.

"These findings are interesting, but the implications for public health and healthcare will only become clear with additional research," said co-author Mmbaga of the Kilimanjaro Clinical Research Institute. "We need to understand how milk immune responses are affected by things we can design public health programs around, like HIV infection or malnutrition."

This research may have applications that go beyond infancy and breastfeeding. Figuring out how the immune system has evolved to strike a balance between protection and harm could help shed light on health problems from infant diarrhea and pneumonia to autoimmune diseases.

"Too often, we implicitly assume that immune responses to separate stimuli are entirely separate—as though the immune system's ability to respond to a dangerous infectious agent doesn't have any implications for its ability to tolerate something that's beneficial or benign, where the response is likely to do more harm than good," Wander noted. "Clues that this isn't the case are accumulating, though, including this study."

More information: Katherine Wander et al, Tradeoffs in milk immunity affect infant infectious disease risk, *Evolution, Medicine, and Public Health* (2022). DOI: 10.1093/emph/eoac020

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