Fecal pH: A Window Into The Infant Gut Microbiome

Tracy Shafizadeh, PhD

The gut microbiome plays an active role in human immune function and metabolism, and the composition of the gut microbiota is a factor in overall health or disease. This active role begins the first day of life, as the infant gut microbiome plays a particularly important role in digestion of human milk as well as early immune programming.[1,2] The organisms that comprise the infant gut microbiome are initially acquired at birth and differ dramatically depending on birth mode and infant diet.[3,4] Additionally, hospitalized infants are known to acquire gut microbes from the hospital environment, including pathogens linked to negative health outcomes such as necrotizing enterocolitis and late onset sepsis.[5] In clinical practice, a detailed compositional analysis of the infant gut microbiome is often unavailable. However, data now show that fecal pH is directly linked to the composition of the gut microbiome and may be a useful tool to evaluate infant gut dysbiosis.

The Infant Gut Microbiome and Fecal pH

It is estimated that many hospitalized infants are dysbiotic, a term that is used to describe an overgrowth of pathogenic bacteria in the gut. Pathogenic and opportunistic bacteria have greater potential to colonize and thrive in environments with elevated pH, 5.5 and above. Conversely, an abundance of protective *Bifidobacterium* in the infant gut has been correlated with a lower pH, ~5.0, creating an environment that is inhospitable to pathogen growth.[6] The infant-specific bacterial species *Bifidobacterium longum* subspecies *infantis* (*B. infantis*) is known to thrive in the breastfed infant gut, where it efficiently converts human milk oligosaccharides (HMOs) present in breastmilk into lactate and acetate, effectively lowering the colonic pH to ~5.0.[7] When the colonic environment is maintained at a more acidic pH, pathogen growth is suppressed, a natural mechanism called colonization resistance.[8]

Reestablishing *B. infantis* Restores Colonization Resistance to the Infant Gut

As most hospitalized infants are found to be dysbiotic due to C-section delivery, premature birth, and exposure to antibiotics, intervention is often needed. When *B. infantis* is missing in the infant gut, clinical studies show that there is elevated pathogen abundance, higher levels of antibiotic resistant bacteria, increased breakdown of the colonic mucin layer and significantly higher levels of enteric inflammation.[7,9,10,11] However, when *B. infantis* colonizes the infant gut during the first months of life, dramatic beneficial effects are observed in both the microbiome composition as well as intestinal biochemistry, resolving the negative effects observed in its absence. As described above, *B. infantis* is uniquely adapted to metabolize HMO, and in turn, prevents the loss of these breastmilk components through fecal excretion. In a recent intervention trial, breastfed term infants who were fed and subsequently colonized with an activated strain, *B. infantis* EVC001 (Evivo), showed a 10-fold reduction in fecal excretion of HMO compared to breastfed infants who were lacking this bacterium.[7] The metabolism of HMO by *B. infantis* EVC001 in the infant gut leads to a subsequent production of lactate and acetate, which serve as fuel for the colonocytes, as well as reduce the pH of the intestinal environment. In the same study, lower colonic pH was associated with reduction of potential gut pathogens as much as 80% compared to breastfed controls. Taken together, colonization of *B. infantis* EVC001 in the infant gut is thought to create a functional and protective environment, reducing the abundance of pathogenic bacteria, and maximizing the utilization of breastmilk nutrients.

Published literature shows a trend of increasing infant fecal pH over the last 100 years, correlating with a loss of *Bifidobacterium* in the infant gut.[6] Infant fecal pH above 5.5 suggests a loss of colonization resistance, leading to functional changes that include increased pathogen abundance, degradation of the gut mucosal barrier, and enteric inflammation. Based on this growing body of evidence linking infant gut microbiome composition, fecal pH and health outcomes, LabCorp of America national diagnostic lab has recently recognized the need for an infant-specific fecal pH reference range and updated the range accordingly to pH 4.5-5.5 for infants 0-6 months of age. Therefore, this simple, non-invasive clinical test provides a window into gut microbiome composition, and may be considered as a tool in detecting infant gut dysbiosis.

Dr Tracy Shafizadeh is a nutritional scientist and the Director of Scientific Communications at Evolve BioSystems.

References

1 Zivkovic, Angela M., et al. "Human milk glycobiome and its impact on the infant gastrointestinal microbiota." Proceedings of the National Academy of Sciences 108. Supplement 1 (2011): 4653-4658.

2 Olin, A.; Henckel, E.; Chen, Y.; Lakshmikanth, T.; Pou, C.; Mikes, J.; Gustafsson, A.; Bernhardsson, A.K.; Zhang, C.; Bohlin, K.; et al. Stereotypic Immune System Development in Newborn Children. Cell 2018, 174, 1277–1292.e14.

3 Duar, R.M.; Kyle, D.; Tribe, R.M. Reintroducing B.infantis to the Cesarean-born neonate: An ecologically sound alternative

to “vaginal seeding”. FEMS Microbiol. Lett. 2020, 367, fnaa032.
4 Ferretti, P.; Pasolli, E.; Tett, A.; Asnicar, F.; Gorfer, V.; Fedi, S.; Armanini, F.; Truong, D.T.; Manara, S.; Zolfo, M.; et al. Mother-to-Infant Microbial Transmission from Different Body Sites Shapes the Developing Infant Gut Microbiome. Cell Host Microbe 2018, 24, 133–145.
5 Brooks, Brandon, et al. “Strain-resolved analysis of hospital rooms and infants reveals overlap between the human and room microbiome.” Nature communications 8.1 (2017): 1-7.
6 Henrick, Bethany M., et al. “Elevated fecal pH indicates a profound change in the breastfed infant gut microbiome due to reduction of Bifidobacterium over the past century.” MSphere 3.2 (2018).
7 Frese, Steven A., et al. “Persistence of supplemented Bifidobacterium longum subsp. infantis EVC001 in breastfed infants.” MSphere 2.6 (2017): e00501-17.
8 Duar, Rebbeca M., David Kyle, and Giorgio Casaburi. “Colonization Resistance in the Infant Gut: The Role of B. Infantis in Reducing pH and Preventing Pathogen Growth.” High-throughput 9.2 (2020): 7.
9 Casaburi, Giorgio, et al. “Early-life gut microbiome modulation reduces the abundance of antibiotic-resistant bacteria.” Antimicrobial Resistance & Infection Control 8.1 (2019): 131.
10 Karav, Sercan, Giorgio Casaburi, and Steven A. Frese. “Reduced colonic mucin degradation in breastfed infants colonized by Bifidobacterium longum subsp. infantis EVC001.” FEBS open bio 8.10 (2018): 1649-1657.
11 Henrick, Bethany M., et al. “Colonization by B. infantis EVC001 modulates enteric inflammation in exclusively breastfed infants.” Pediatric research 86.6 (2019): 749-757.