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EDITORIAL

Another reason to favor exclusive breastfeeding: microbiome resilience☆,☆☆

Outro motivo para incentivar aleitamento materno exclusivo: resiliência do microbioma

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Knowledge of the human microbiome has rapidly accelerated thanks to the Human Microbiome Project and the increasing availability of culture independent high-throughput sequencing technology. With these new tools, we have come to appreciate the extensive complexity and dynamics of the human microbiome, particularly the one which colonizes our gastrointestinal tract. While some studies appear to suggest a rather chaotic, random establishment of the human gut microbiome early in life, the latest research seems to suggest a carefully planned design based on the co-evolutionary integration of our genome composition and function with the epigenetic influence of the symbiotic microbiome. Therefore, any departure from the evolutionary plan on how proper microbiome engraftment should occur, including maternal lifestyle and diet, mode of delivery, feeding regimen, exposure to antibiotics, and home environment,[1,2] just to name a few, may have potentially detrimental clinical consequences. Indeed, there is now evidence suggesting that the microbiome-mediated maturation of epithelial barriers and gut-associated lymphoid tissue (GALT) impacts the capacity of the host to develop responses that maintain normal homeostasis and prevent aberrant pro-inflammatory or allergic responses. This implies that disruptions in the development of a healthy microbiome ecosystem early in life can have lasting effects.[3]

Establishment of a healthy microbiome may begin even before birth. Despite a longstanding belief that the fetus resides in a sterile environment, recent studies have revealed microbiota in both the placenta[4] and meconium.[5] Current mouse models suggest that presentation of maternal commensal bacterial components to the fetus in the last trimester of pregnancy is a likely mechanism for immune system maturation and oral tolerance.[6] There is growing evidence that exposure to healthy and diverse commensal species early in life confers protection against chronic inflammatory diseases (CIDs). Technology now allows for vast and sophisticated study of the human microbiome (microbes present in the human host and their functions), the

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metagenome (DNA extracted from samples and their functions), the metatranscriptome (total content of gene transcripts, as RNA, and their functions), and the metabolome (presence and function of metabolites). As the field expands exponentially in the wake of non-culture-based technologies to study the microbiome, a multi-omic systems biology research approach in pediatrics has the potential to revolutionize our understanding of many of the most common diseases that children face. Among the many variables studied so far, early feeding regimens seem to have a strong impact on proper microbiome engraftment and function.

In this issue of the Jornal of Pediatria, Carvalho-Ramos et al. present some intriguing data suggesting that, besides the already described beneficial effect of exclusive breastfeeding on gut microbiome composition through probiotic and prebiotic imprinting, another additional advantage, namely increased microbial community resilience, seems to favor exclusive breastfeeding over mixed feeding for the first six months.[7] By sampling stools from 11 infants monthly during their first year of life, the authors showed a rather stable pattern of microbiome evolution over time among children exclusively or predominantly breastfed compared to those children with a mixed feeding regime that included non-human milk and early solid food introduction, even if there was a high intra-subject variability. The most intriguing finding was an uninterrupted ecological succession despite the influence of external factors, such as introduction of solid food (complementary feeding) and/or antibiotic administration in breastfed, but not in mix-fed babies.[7] These results suggest that the gut microbiome of breastfed infants has the capability of resisting external perturbations by re-establishing the ecological milieu that was present before the exposure to the perturbing factor(s).

While these results are intriguing, and even more so because they were generated in children belonging to impoverished mothers in an urban area in Brazil and, therefore, more susceptible to a variety of infectious diseases, the small number and the descriptive nature of this study should raise some caution in jumping to definitive conclusions. Theoretically, if inappropriate microbiota composition (dysbiosis) increases the susceptibility to developing disease, then influencing its composition and resilience by promoting specific early feeding practices should contribute to an improvement in microbiome health, and thereby to disease modulation or even prevention. However, the depth of our understanding of the microbiome's contribution to disease remains shallow. We believe that a healthy microbiome is one that is diverse, and indeed there are multiple studies showing that a lack of microbiome diversity is associated with many diseases. Yet, we continue to focus our efforts simply to understand what constitutes a ''normal'' microbiome.[8]

Mechanistic work suggesting that certain specific gut microbiota compositions may contribute to the improvement of intestinal health has been done largely without accounting for the complex biological networks known to contribute to disease development. Research going forward must focus on identifying specific microbiota signatures associated with disease development before any conclusions can be drawn on what constitutes a ''healthy microbiome.'' Nevertheless, for promising translational medicine to be possible, we need to transition from descriptive to mechanistic studies of the microbiome. Given the hypothesis that the development of the microbiome during the first 1,000 days of life has a lasting effect on an individual's future health and risk of disease, pediatric studies like the one from Carvalho-Ramos and coworkers, if well designed and powered, are particularly well positioned to lead this transition.

Conflicts of interest

The author declares no conflicts of interest.

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