Follow your gut: How farms protect from childhood asthma

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Asthma impacts millions of children at a young age, but children growing up on a farm have a lower risk of developing asthma than children not living on a farm. The mechanisms behind this protective

farm effect on childhood asthma are largely unknown. A group of researchers from Helmholtz Zentrum München and the Dr. von Hauner Children's Hospital of Ludwig Maximilians University Munich (LMU) clarified how the children's gut microbiome is involved in the protection process.

We are born into an environment full of small organisms called microbiota. Within the first minutes and hours of our lives, they start challenging, but also educating, our immune system. The largest immune organ is our gut, where maturation of the immune system and maturation of the colonizing bacteria, the gut microbiome, go hand in hand. After profound perturbations in the first year of life, the maturation process, the composition of the gut microbiome gradually stabilizes and accompanies us for our lives. Previous research of the Munich scientists showed an asthma-protective effect by a diverse environmental microbiome, which was particularly pronounced in farm children. The question now was whether this effect could be attributed to the maturation process of the early gut microbiome.

Farm life boosts gut microbiome maturation in childrenThe researchers analyzed fecal samples from more than 700 infants partly growing up on traditional farms between the age of 2 and 12 months who took part in PASTURE—a European birth cohort, which runs for almost 20 years now with funding from the European Commission.

"We found that a comparatively large part of the protective farm effect on childhood asthma was mediated by the maturation of the gut microbiome in the first year of life" states Dr. Martin Depner, biostatistician at Helmholtz Zentrum München, and further concludes: "This suggests that farm children are in contact with environmental factors possibly environmental microbiota that interact with the gut microbiome and lead to this protective effect."

The researchers anticipated effects of nutrition on the gut microbiome maturation but were surprised to find strong effects of farm-related exposures such as stays in animal sheds. This emphasizes the importance of the environment for the protective effect. In addition, vaginal delivery and breastfeeding fostered a protective microbiome in the first two months of life.

Furthermore, the researchers discovered an inverse association of asthma with measured level of fecal butyrate. Butyrate is a short chain fatty acid which is known to have an asthma protective effect in mice. The researchers concluded that gut bacteria such as Roseburia and Coprococcus with the potential of producing short chain fatty acids may contribute to asthma protection in humans as well. Children with a matured gut microbiome showed a higher amount of these bacteria (Roseburia and Coprococcus) compared to other children.

"Our study provides further evidence that the gut may have an influence on the health of the lung. A mature gut microbiome with a high level of short chain fatty acids had a protective effect on the respiratory health of the children in this study. This suggests the idea of a relevant gut-lung axis in humans", says Dr. Markus Ege, professor for clinical-respiratory epidemiology at the Dr. von Hauner Children's Hospital. "This also means, however, that an immature gut microbiome may contribute to the development of diseases. This emphasizes the need for prevention strategies in the first year of life, when the gut microbiome is highly plastic and amenable to modification."

Probiotic prevention strategiesThe researchers demonstrated that the asthma protective effect is not dependent on one single bacteria only, but on the maturation of the entire gut microbiome. This finding questions the approach of using single bacteria as probiotics for the prevention of asthma. Probiotics should rather be tested with respect to their sustained effect on the compositional structure of the gut microbiome and its

maturation early in life.

Further studies on cow milkNutritional aspects analyzed in this study may serve as prevention strategies such as consumption of cow's milk. Unprocessed raw milk, however, cannot be recommended because of the risk of life-threatening infections such as EHEC. Scientists at the Dr. von Hauner Children's Hospital are currently running a clinical trial on the effects of minimally processed but microbiologically safe milk for the prevention of asthma and allergies (MARTHA trial).

Helmholtz Zentrum MünchenHelmholtz Zentrum München is a research center with the mission to discover personalized medical solutions for the prevention and therapy of environmentally-induced diseases and promote a healthier society in a rapidly changing world. It investigates important common diseases which develop from the interaction of lifestyle, environmental factors and personal genetic background, focusing particularly on diabetes mellitus, allergies and chronic lung diseases. Helmholtz Zentrum München is headquartered in Neuherberg in the north of Munich and has about 2,500 staff members. It is a member of the Helmholtz Association, the largest scientific organization in Germany with more than 40,000 employees at 19 research centers.

The study is published in *Nature Medicine*.

More information: Maturation of the gut microbiome during the first year of life contributes to the protective farm effect on childhood asthma, *Nature Medicine* (2020). DOI: 10.1038/s41591-020-1095-x , www.nature.com/articles/s41591-020-1095-x

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