

## CORRESPONDENCE



## Farm Microbiome and Childhood Asthma

**TO THE EDITOR:** Ege et al. (Feb. 24 issue)<sup>1</sup> report that in two cross-sectional studies, children who lived on farms and were exposed to an increased range of microbes had a reduced incidence of asthma. However, this conclusion might be skewed by a confounder that the authors did not consider. Several studies<sup>2,3</sup> have shown that breast-feeding is protective against asthma, and children who live on farms are more likely to be breast-fed for longer than children who do not live on farms. In a large American study, 64% of farm mothers were likely to have breast-fed their first baby, as compared with 49% of other mothers.<sup>4</sup> Notably, both prolonged breast-feeding and exposure to farm animals in early life were strongly correlated with a reduced incidence of childhood non-Hodgkin's lymphoma.<sup>5</sup> Future studies examining possible correlations between early childhood microbial exposures, farm living, and asthma, as well as other immune disorders, must therefore include breast-feeding as an added confounder.

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No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** Ege et al. report that a diversity of microbial exposure, as measured in samples of mattress dust or settled dust from children's rooms, was inversely related to the prevalence of asthma. However, the authors do not account for extraneous confounders that could be related to both asthma risk and diversity of environmental microbial exposure, such as gastrointestinal microbial colonization during early childhood. In studies that were based on a U.S. sample from the National Health and Nutrition Examination Survey, we found that seropositivity for *Helicobacter pylori* was inversely associated with an onset of asthma before the age of 5 years and with current asthma in children between the ages of 3 and 13 years.<sup>1</sup> Among adults, there was an inverse relationship between the presence of the most interactive strain of *H. pylori* (cagA+) and a history of asthma, and the inverse association was stronger for asthma with an onset before the age of 15 years.<sup>2</sup> These findings were mirrored in

## THIS WEEK'S LETTERS

- 1972 Farm Microbiome and Childhood Asthma
- 1973 AIP Mutation in Pituitary Adenomas
- 1976 Hypoxia and Inflammation
- 1978 Radioiodine Therapy for Hyperthyroidism
- 1979 More on NK-Cell and B-Cell Deficiency with a Thymic Mass
- 1981 Anaphylaxis from Passive Transfer of Peanut Allergen in a Blood Product

a case-control study.<sup>3</sup> Future studies should consider exposures to both environmental (exogenous) microbes and to endogenous microbes that are disappearing, such as *H. pylori*.<sup>4</sup>

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No potential conflict of interest relevant to this letter was reported.

1. Chen Y, Blaser MJ. *Helicobacter pylori* colonization is inversely associated with childhood asthma. *J Infect Dis* 2008;198:553-60.
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**THE AUTHORS REPLY:** Gurwitz and Lunshof suggest that breast-feeding is a potential confounder in the association between living on a farm and asthma or atopy. They quote a study conducted in America in the 1970s that showed increased rates of breast-feeding among mothers who live on farms.<sup>1</sup> In contrast to that study, mothers in Central Europe who live on farms tend to breast-feed their children for shorter periods than mothers from the same rural regions. In our analysis, the association between living on a farm and exclusive breast-feeding for at least 5 months was inverse in both populations that we studied. In the PARISAL (Prevention of Allergy — Risk Factors for Sensitization in Children Related to Farming and Anthroposophic Lifestyle) study, the odds ratio for exclusive breast-feeding was 0.40 (95% confidence interval [CI], 0.33 to 0.48), and in GABRIELA (Multidisciplinary Study to Identify the Genetic and Environmental Causes of Asthma in the European Community), the odds ratio was 0.85 (95% CI, 0.77 to 0.94). The associations between living on a farm and asthma or atopy were not confounded either by breast-feeding for at least 6 months or by exclusive breast-feeding for

at least 5 months. Therefore, we did not adjust our analyses for breast-feeding.

Chen and Blaser comment that we did not account for gastrointestinal microbial colonization during early childhood as a potential confounder in the association between asthma and the diversity of environmental microbial exposure. Unfortunately, data on gastrointestinal microbial colonization in early childhood were not available in our data set. However, gastrointestinal microbial colonization is unlikely to confound the association for several reasons. Since the association between bacterial diversity and asthma was strong, with an odds ratio of 0.62 for each additional 10 bands indicating more microbial diversity, the contribution of the gastrointestinal flora to the diversity would need to be extremely large. Furthermore, most bacteria that were identified in the children's mattresses were non-pathogenic environmental bacteria. A study involving young adults in rural Germany did not reveal an association between farm exposures and seropositivity for *H. pylori*.<sup>2</sup> For these reasons, we do not consider gastrointestinal microbial colonization to be a relevant confounder for the association between microbial diversity and asthma. However, this conclusion does not contradict the hypothesis that *H. pylori* has an independent asthma-protective potential, as suggested by Chen and Blaser, who assessed *H. pylori* seropositivity without adjustment for other microbial exposures.<sup>3</sup>

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Since publication of their article, the authors report no further potential conflict of interest.

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## AIP Mutation in Pituitary Adenomas

**TO THE EDITOR:** Chahal et al. (Jan. 6 issue)<sup>1</sup> describe four families with familial isolated pituitary adenomas who had the same mutation as

an 18th-century giant.<sup>2</sup> They conclude that the old theory that considered gigantism to be a congenital disorder, whereas acromegaly was consid-