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Innate Immunity and Asthma Risk

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The authors reply

Cooper asks whether differences in asthma prevalence between Amish and Hutterites may derive from the increased use of antibiotics by humans and livestock among the Hutterites, both of which may affect the human microbiome. George further asks whether fecal or lung microbiota may protect the Amish from asthma by preventing viral lower respiratory tract illnesses. Finally, Nadelman notes that the larger Hutterite farms may rely on diesel-powered tractors and diesel-powered or gasoline-powered vehicles whose emissions may increase airway inflammation and account for the higher rates of asthma observed among the Hutterites than among the Amish, who use horses to plow their fields.

We agree with the authors that these questions are pertinent and consistent with published literature, but unfortunately we did not assess these exposures in our study. Instead, we focused on the indoor environment. Our demonstration that administration to mice of airborne dust collected in Amish and Hutterite homes was sufficient to protect from or enhance experimental asthma, respectively, and result in immune profiles consistent with those seen in Amish and Hutterite children supports an important contribution of this environment to the different rates of asthma in these populations.

On the other hand, we have observed that unlike Amish children, young Hutterite children typically do not spend time near farm animals or in the barns, which are much larger and located at much greater distances from their homes than are Amish barns. We hypothesized, therefore, that Hutterite children are not exposed in early life to the asthma-protective factors that have been identified in the European epidemiologic studies of farming (farm animals, hay, and straw)^{1–3} and to which the Amish children are abundantly exposed. We directly tested this hypothesis by examining the effects of barn-dust extracts in a mouse model. Indeed, inhalation of Hutterite barn-dust extract was sufficient to inhibit house-dust mite–induced airway hyper-responsiveness, eosinophilia in the bronchoalveolar lavage (Fig. 1), and the elevation of house-dust mite–specific IgE levels (data not shown), and to induce neutrophilia in the bronchoalveolar lavage, as effectively as inhalation of Amish barn-dust

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extract. Hutterite barn-dust extract also conferred similar protection in an ovalbumin model (data not shown). Therefore, an environment with robust asthma-protective properties appears to exist within the Hutterite colonies, but Hutterite children are not exposed to this environment in early life.

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Figure 1. Protection against Allergen-Induced Experimental Asthma by Dust from Amish and Hutterite Barns

Amish or Hutterite aqueous barn-dust extracts (5 mg of dust equivalent in 50 μ l per treatment for a total of 14 treatments) were instilled intranasally every other day from day – 10 to day 21 into adult (6-to-7-week-old) BALB/c mice that received house-dust mite extract (HDM) (Greer, 100 μ g) intranasally on days 0, 7, 14, and 21. Airway resistance (shown as centimeters of water per milliliter per second and stimulated in response to increasing doses of acetylcholine administered intravenously) (Panel A) and bronchoalveolar-lavage cellularity (Panel B) were measured on day 22, as described in our article. Hutterite barn-dust extracts were prepared as described in our article. The results are for two experiments involving six to nine mice per group. Statistical differences in experimental measures were assessed with the use of a mixed-effects model for repeated measures (Panel A) and Student's t-test (Panel B). I bars represent the standard error. PBS denotes phosphate-buffered saline.