

Results of the US Third National Health and Nutrition Examination Survey support the hygiene hypothesis

To the Editor:

We have read with interest the article by Sheikh et al¹ regarding the relation between T_H2-mediated atopy and T_H1-mediated autoimmune disorders among adult subjects included in the US Third National Health and Nutrition Examination Survey. They found no evidence of an inverse relation between atopy and patient reports of physician-diagnosed common autoimmune disorders; in contrast, physician-diagnosed allergic disorders were positively associated with physician-diagnosed autoimmune diseases. Based on these findings, the authors concluded that the T_H1/T_H2 paradigm might be an oversimplification and that the results provide no support for the hygiene hypothesis.

The coexistence of T_H1-mediated and T_H2-mediated disorders in the same population was demonstrated by other reports. Kero et al,² by using data from the Finnish Medical Birth Register, found that the cumulative incidence of asthma in children with celiac disease or rheumatoid arthritis was significantly higher than in

children without celiac disease or rheumatoid arthritis; furthermore, asthma tended to be more common in children with type 1 diabetes than in children without type 1 diabetes. Moreover, a positive correlation between asthma prevalence and incidence of type 1 diabetes was demonstrated at the population level. Taken together, these epidemiologic data suggest that common factors underlie the development of either T_H1 -mediated or T_H2 -mediated disorders. As we recently suggested elsewhere, an important factor facilitating the onset of either allergic or autoimmune disorders might be the reduced exposure to infectious agents in early childhood, which might exert a profound impact on the developing immune system and facilitate inappropriate responses against allergens or autoantigens.

The data from the US Third National Health and Nutrition Examination Survey were also examined by Matricardi et al,³ who found an association between the serologic evidence of acquisition of certain infections acquired by the fecal-oral route or by food-borne toxins and a lower probability of having allergic rhinitis and asthma. The authors concluded that hygiene is a major factor contributing to the increase in allergic rhinitis, asthma, and atopic sensitization in Westernized countries, but they did not analyze the relation with autoimmune disorders.

Taken together, these data are in line with the results by Sheikh et al because they simply do not support the explanation advocated for the hygiene hypothesis, which is to say that the lack of infection breaks the balance between T_H2 - and T_H1 -mediated immune responses and facilitates T_H2 responses against allergens. The findings of Sheikh et al demonstrate that T_H1 - and T_H2 -mediated disorders are not mutually exclusive and, in contrast, are positively associated. This reinforces the possibility that common factors underlie allergic and autoimmune disorders and speaks in favor of the hygiene hypothesis, intended as increased risk of immune-mediated disorders when the exposure to infectious agents is low, in particular during childhood.

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Reply

To the Editor:

Our finding that patient reports of physician-diagnosed T_H1 and T_H2 disorders are positively associated has at least two possible explanations. The first is that these findings simply reflect information biases (physician diagnosis and/or patient recall), whereas the second, and more interesting possibility, as raised by Airaghi and Tedeschi¹ and discussed at some length in our original report, is that this may possibly reflect the impact of environmental influences on the developing immune system, resulting in increased risk to both allergic and autoimmune disorders. A prospective cohort study investigating the impact of early life influences (such as exposure to childhood infections) is, we believe, an important next step to help untangle these possible explanations and, importantly, to allow temporal and dose-response relation between environmental factors and disease onset to be studied.

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