

study is important for possible future analyses. To the best of our knowledge, the data from single nucleotide polymorphism-based studies of asthma genetics have not been subjected to meta-analysis, which considers data from several studies and provides for global interpretation of the data. Meta-analysis has successfully identified variants having modest effects on diseases such as diabetes and schizophrenia.³ Collections of genotype data from different studies will help to identify variants associated with the development of asthma and atopy.

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Is the "hygiene hypothesis" being challenged?

To the Editor:

I read with great interest the epidemiologic study reported by Sheikh, Smeeth, and Hubbard in the Journal entitled "There is no evidence of an inverse relationship between T_H2-mediated atopy and T_H2-mediated autoimmune disorders: lack of support for the hygiene hypothesis."¹

Although the authors used a careful statistical analysis on retrospectively collected epidemiologic data, a shortcoming of the interpretation should be pointed out. The authors explained the limitation of their study in the discussion, but the study deserves comments because the authors seemed to overlook several issues.

First, there is a clear difference in the natural course of T_H1-mediated and T_H2-mediated diseases. T_H1-mediated atopic allergic disorders occurred in younger ages even before they reached school age. In contrast, T_H1-mediated diseases such as type 1 diabetes, rheumatoid arthritis, or thyroid disorders as cited in the study occurred more often in teenaged or older individuals. As the majority of responders of the study were adults (some older than 81 years), the accuracy of the report on the diseases that occurred in early childhood is always suspect. As we examined the list of questions on the autoimmune diseases, the questions addressed to the responders are not clear enough to separate if the responders had type 1 dia-

betes or type 2 diabetes. Only the former is considered a T_H1 disease. To separate these two conditions, more information is needed. For instance, most of the patients with type 1 diabetes would have laboratory markers such as the presence of islet cell antibodies.^{2,3} Likewise, when the authors listed arthritis questions, were differences between juvenile rheumatoid arthritis and adult arthritis stated? Also, which thyroid disease was discussed? Not all thyroid diseases have an autoimmune basis. Those important questions are missing in the study.

Second, the lack of information concerning the age of onset of the diseases mentioned in the study makes the conclusion of the study somewhat tenuous. T_H2-mediated allergic disorders start early, and the immunologic process could be long-lasting but may be outgrown as the age progresses. Thus, the pathologic process (allergic inflammation) would tend to persist longer or may terminate at some point. In contrast, T_H1 disease is a permanent end-organ disease, but its immunologic process may end when the end-organ is completely destroyed. In the case of type 1 diabetes, all the islets may disappear after 5 to 8 years.^{2,3} It would reach the point that the immunologic process is no longer active and yet the disease is permanently established. This is also evidenced by the gradual disappearance of the laboratory markers indicating that the antibody-mediated process or cell-mediated process in autoimmune diseases is fading.^{2,3} When that occurs, the T_H2 immune mechanism may again become dominant. In other words, allergic diseases may occur after the T_H1 immunologic process becomes weaker. Thus, the information on the onset of the disease is critical, and the T_H1/T_H2 paradigm needs to be explained in the context of a dynamic process in a set time frame (as within certain age group) and not to be interpreted as an inflexible "either, or" process.

Third, the hygiene hypothesis is originally proposed to explain if the early exposure of infectious agents or endotoxin in childhood could influence the onset of T_H2 diseases.⁴ In part, it is proposed to explain the increasing incidence of allergic disorders in children in well-developed industrial countries. It is postulated that early infections in children may serve to trigger a T_H1 immunologic process, thus shielding them from influence of the T_H2 immunologic process. I do not believe that the hypothesis was ever promoted to predict the onset of T_H1 diseases as the authors seemed to imply.

Clearly, the hygiene hypothesis triggers an interesting debate among researchers and clinicians alike throughout the world. In the heat of discussion, however, we sometimes tend to perceive the T_H1/T_H2 paradigm as a life-long, inflexible process instead of viewing it as a dynamic one that perhaps has meaning in the different age groups, especially in children. A better-designed prospective study, started from childhood, will help us understand the complex immunologic responses in the host in the different environments.

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Reply

To the Editor:

We are grateful to Dr Huang¹ for his observations on our article.² In response, we would like to reiterate that to minimize the possible effect of information bias, we chose not to rely on recall of atopic disease for the primary analysis and instead used a more objective contemporaneous definition that was based on skin prick test results. Regarding the relationship between atopic diseases and autoimmune disease history, there was, as we discussed in the article, likely to have been some ascertainment bias, which might have resulted in the observed positive association in our secondary analysis examining the relationship between atopic and autoimmune disease history.

Huang raises a number of concerns regarding the possibility of misclassification of those with a history of autoimmune disease. In relation to his point about the misclassification of type 1 and type 2 diabetes, we believe that this is likely to have happened in only a very few cases. This is because our definition of type 1 diabetes was based on current use of insulin but no use of oral diabetic drugs; the vast majority of people with diabetes treated only with insulin are likely to have type 1 disease. Misclassification of those with rheumatoid arthritis is also unlikely because there was a specific question asked in the NHANES III survey with the explicit aim of differentiating between rheumatoid arthritis and osteoarthritis. Although not all thyroid disease is autoimmune in origin, the large majority is, and any misclassification errors are therefore likely to be relatively few and are, as a consequence, unlikely to have altered the conclusions.

We do, however, concur with Huang that in our study we were focusing on adult outcomes in the relationship between T_H1 - and T_H2 -mediated disorders. Changes in the relationship between these conditions could well have occurred before the survey, but studying these would, as the author states, require a long-term cohort follow-up study from an early age.

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High-efficiency particle arrest vacuums and cat allergen exposure

To the Editor:

The recent article by Gore et al¹ in the April issue of the Journal presents data that demonstrate significant disparity between field and experimental chamber vacuuming, regardless of whether new high-efficiency particle arrest (HEPA) or older microfilter-containing vacuum cleaners were used. On the basis of these differences, the authors conclude that the best advice to cat owners is to remove the cat from the home. Several concerns about the methodology and the authors' interpretation of the data require clarification.

First, the experimental chamber used a finite amount of cat allergen (36 mg), and the room air was continuously being filtered with a HEPA filter, which might in part explain the differences between the 2 test conditions. Second, the authors do not clearly delineate baseline cat allergen levels in the carpets of field homes being tested, the cleaning practices of the residents over time, or other housing characteristics, all of which might have affected the results. If baseline cat allergen levels in the homes were significantly greater than in the experimental chamber, dispersion of allergen into the air by the vacuuming process itself could have been significantly increased well above airborne levels in the experimental chamber.

The authors conclude that HEPA vacuum cleaners are inadequate as an intervention in cat-sensitized homeowners and that the treatment of choice is removal of the cat from the home.¹ Although no one would dispute this latter statement, most clinical allergists recognize the futility of this recommendation. Approximately one third of the US population owns a cat, and most atopic individuals refuse to comply when asked to remove the cat from the home.² Therefore clinicians need to develop alternative ways in which cat-sensitized individuals can coexist with their pets. The data presented by Gore et al¹ reveal important insights into real-life exposures that can only be resolved by means of further remediation-health outcome studies. van der Heide et al³ previously demonstrated that multiple interventions (bedding encasements