To the Editor:

We thank the authors for their thoughtful comments. To address their concerns that our results may be explained by β2-adrenergic receptor downregulation in the asthmatic population, we measured β2-adrenergic expression in PBMCs from the original asthmatic group and the healthy control group by real-time PCR. Total RNA was isolated from PBMCs according to the manufacturer’s guidelines (Qiagen, Valencia, Calif), transcribed into cDNA, and analyzed by real-time PCR by using the dual-labeled fluorogenic probe method on an ABI Prism 7000 sequence detector (Applied Biosystems, Foster City, Calif). Primers and probes for the human β2-adrenergic receptor and 18S RNA were purchased from Applied Biosystems. A standard curve was generated by using the fluorescent data from 10-fold serial dilutions of total RNA of the corresponding 18S RNA levels in each sample. Quantities of β2-adrenergic receptor in test samples were normalized to the corresponding 18S RNA levels in each sample.

As shown in Fig 1, no differences were detected in the amount of β2-adrenergic receptor expression: 2.281 ± 966.0 ng/ng 18S RNA versus 1693 ± 486.8 ng/ng 18S RNA in the asthmatic and control groups, respectively. Therefore, it does not seem that the differences in PBMC responses to the low-dose fluticasone/salmeterol combination between the asthmatic and healthy control groups can be explained by β2-adrenergic receptor downregulation in the asthmatic population. We thank the authors for bringing the error in the figure legends for Fig E2 and Fig 3 to our attention. The correct figure legends are as follows:

FIG E2. Inhibition of PHA-induced IFN-γ and TNF-α production by suboptimal concentration of fluticasone (10⁻¹² mol/L) in combination with salmeterol in PHA-stimulated supernatants from the healthy control group (A and C) or the allergic asthmatic group (B and D) (*P < .05 and **P < .01 as compared with PHA only).

FIG 3. Secretion of IL-13 (A and B) and IL-5 (C and D) in mitogen-stimulated cell cultures from patients with allergy and asthma in the presence of fluticasone or low-dose fluticasone/salmeterol combinations (***P < .001 and **P < .05 compared with PHA only).

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REFERENCE


Origins of atopy in pediatric asthma

To the Editor:

In their interesting article, Heyman et al describe an interaction of respiratory viral infection and atopy in exacerbations of pediatric asthma, resulting in hospitalization among children aged 3 years and older but not among younger children. I would like to comment on their discussion of potential factors influencing the development of atopy among older pediatric asthmatic patients. They discuss and dismiss the possible roles of previous respiratory syncytial virus infection, exposure to environmental tobacco smoke, and low socioeconomic status. They also briefly consider the potential contribution of mycoplasma and Chlamydia species, stating that the evaluation of these infections remains a challenge (I agree) and that these infections have been detected in only 5% of hospitalized asthmatic patients. I would like to expand on these points.

Although mycoplasma and Chlamydia species are rarely detected in the upper respiratory tract of asthmatic patients, recent studies on bronchoalveolar lavage fluid indicate that Chlamydia pneumoniae can be found in more than 50% of cases of pediatric asthma and other pediatric obstructive lung diseases. Furthermore, C pneumoniae–specific IgE has been associated with pediatric asthma, and even more surprising is the emerging in vitro evidence that raises the possibility that pediatric C pneumoniae infection of human dendritic cells could even bias the developing immune response toward a Th2 phenotype.

In part because of the potential therapeutic applications of these and other related observations, I believe now is the opportune time to advocate for closer collaboration between chlamydiologists with expertise in microbiologic detection and generalist and specialist asthma researchers.

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Reply

To the Editor:

We appreciate the comments from Dr David Hahn, who has previously described the positive association between Chlamydia pneumoniae infection and wheezing, asthmatic bronchitis, and the onset of asthma in adults. As pointed out by Dr Hahn, the role of C pneumoniae in the cause of asthma and allergic inflammation in the lungs is not easy to evaluate. On the basis of current information, it is still difficult to determine whether C pneumoniae infection in the lower airways of children with symptomatic asthma is a common problem. Although the detection of viable C pneumoniae reported in bronchoalveolar lavage fluid from asthmatic children in the study by Webley et al is of interest, bronchial lavage is rarely indicated or performed in children with asthma. For this reason, it would be important to know the clinical status and characteristics of the children who underwent this procedure in greater detail to judge the relevance of the results to the general population. In the study by Emre et al, referenced by Dr Hahn, positive cultures for C pneumoniae from the nasopharynx (not bronchoalveolar lavage) were detected in 11% of children with wheezing. It is interesting that serum IgE antibody to C pneumoniae was detected by means of immunoblotting in a subset of these patients, but it would be important to confirm these results by using other methods for measuring C pneumoniae-specific IgE antibody. By comparison, a much greater percentage of children with wheezing exacerbations are infected with rhinovirus, which almost all studies indicate is the dominant respiratory tract pathogen linked to acute asthma attacks in children.

In reference to our study, close to half of the children hospitalized for wheezing, ages 3 years and older, were admitted during the fall (September, October, and November). This is a recurrent problem in Virginia. We suspect that this peak in hospitalizations is not significantly associated with acute C pneumoniae infections, which are not known to have an annual fall seasonal pattern. A role for C pneumoniae in the origins of atopy in pediatric asthma is an interesting hypothesis. In this regard, it would be helpful to know, for example, whether children with C pneumoniae induced—lung infections during infancy are more or less likely to become atopic and have asthma as they grow older. We agree with Dr Hahn that studies focused on C pneumoniae infections and the cause of asthma are of interest.

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REFERENCES


Not enough spores?

To the Editor:

We wish to comment on a recent article by Dales et al regarding the effect of outdoor aeroallergens on hospitalization for asthma.

The authors used Rotorod (rotational impaction) samplers and then enumerated the samples for Aeroallergen content at 20 and 40 times magnification (we assume 200× and 400× magnification) by using 15 randomly chosen fields.

We reviewed a number of references cited in the 2002 edition of Multidata’s operating instructions for their Rotorod sampler. We were able to find only one reference2 for reducing the enumerated sample area by using a threshold level of 400 counted pollen grains.

Even though the 15 randomly chosen field enumeration method “had been previously tested,” there is no citation

REFERENCES