

also be the link for increased specific IgE production and peripheral eosinophilia. In the recessive genetic model, a higher percentage of subjects with the TT genotype have atopic asthma, and this supports the importance of TARC in asthma pathogenesis.<sup>3-6</sup> Asthmatic patients homozygous for the T mutant had significantly higher plasma TARC concentrations compared with the CT and CC genotypes, which is consistent with the finding that TARC C-431T was significantly associated with various atopy phenotypes under the recessive but not codominant model. Thus we hypothesize that 2 T alleles have to be present for this SNP to exert any influence on TARC expression. Functional TARC reporter assay is necessary to answer this question.

The allele frequencies of the TARC C-431T allele in this study is lower compared with that seen in Japanese subjects<sup>8</sup>: the allele frequency of T was 27% in our control subjects and 36% in Japanese adult control subjects. The significant difference in genetic epidemiology of TARC C-431T between our southern Chinese subjects and the closely related Japanese subjects is similar to that reported for IL13 R130Q.<sup>10</sup> This finding highlights the importance of replicating genetic association studies in each population rather than generalizing these findings when one tries to establish the relationship between susceptibility genes and complex human diseases, such as asthma and atopy.

In summary, the C-431T polymorphism in the TARC promoter shows a significant association with atopy, house dust mite, and cat sensitization and peripheral eosinophilia in Chinese children. The results of this study support that TARC plays an important role in enhancing T<sub>H</sub>2-mediated allergic inflammation that results in IgE production and eosinophil recruitment.

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## Exhaled air temperature and eosinophil airway inflammation in allergic asthmatic children

To the Editor:

The need to monitor airway inflammation in asthma, particularly in pediatric populations, has led to the development of a number of noninvasive methods of assessment,<sup>1</sup> including analysis of cells and cell products in sputum samples collected by means of induced sputum stimulation,<sup>1-3</sup> as well as the measurement of exhaled markers<sup>1-3</sup> and soluble mediators obtained from exhaled breath condensates.<sup>1-5</sup> Recently, exhaled air temperature has also been suggested as a noninvasive method for the evaluation of airway inflammation in asthma.<sup>6,7</sup> The present study was performed to determine the utility of measurement of exhaled air temperature changes in a group of mite-sensitive asthmatic children as a predictive marker of lung inflammation, as determined on the basis of eosinophil content in hypertonic saline-induced sputum samples from these children.

Thirteen mite-sensitized asthmatic children (8-15 years of age) were evaluated on the day of the entry to the residential house "Istituto Pio XII" (Misurina BL) at 1756 m in the Italian Alps, an environment free of mite allergen because of its location at a high altitude. The study was approved by the Istituto Pio XII Ethics Committee, and informed consent was obtained from the children, as well as their parents. The children had been living with their families for at least a 3-month period before their admission to the residential home. An initial baseline evaluation was performed in September (T0) on entry to the residential home, and a second assessment was performed in December (T1). The study consisted of measurements of exhaled air temperature and sputum induction and was performed out of the pollen season to avoid the confounding effects of outdoor allergens.

At T0, the children were receiving regular treatment with inhaled steroids, either 100 to 200  $\mu\text{g}/\text{d}$  fluticasone or 200  $\mu\text{g}/\text{d}$  budesonide. None of the children received oral steroids during the study.

The temperature of the exhaled air was measured with a high-performance temperature indicator (DP41-TC, Omega Engineering Ltd) connected to a thermocouple (COCO-0.001 Omega Engineering Ltd) during a slow expiratory effort, beginning at total lung capacity through a mouthpiece against a resistance (mouth pressure  $>5$  mm H<sub>2</sub>O) and with a biofeedback used to maintain a 5 to 6 L/min steady flow.<sup>8</sup> The plateau values at the end of the expiration (PLET) were recorded. Three replicate evaluations with samples taken at 5-minute intervals were performed, and the mean of the 2 closest values was considered in the analysis of the results. All measurements were performed early in the morning between 7:30 and 9 AM. The environmental temperature and humidity were controlled in the laboratory where the measurements were performed.

Sputum was induced by means of inhalation of hypertonic saline solution with a standardized method.<sup>3</sup> Differences in exhaled air temperature and sputum percentage eosinophils (September [T0] and December [T1] values) were assessed with the paired Student *t* test. A *P* value of less than .05 was considered significant. Data are presented as means  $\pm$  SEM. At T1, it was not possible to collect adequate sputum samples for analysis in 3 children.

During the time of the study, it was possible to gradually withhold inhaled corticosteroids in all of the children. The eosinophil percentage in sputum samples was  $8.5\% \pm 1.0\%$  at T0 and  $3.8\% \pm 0.4\%$  at T1 (*P* = .0032). Exhaled air temperature (PLET) value was  $29.76^\circ\text{C} \pm 0.42^\circ\text{C}$  at T0 and  $26.36^\circ\text{C} \pm 0.49^\circ\text{C}$  at T1 (*P* = .0001), with environmental temperature of  $21.3^\circ\text{C}$  at T0 and  $20.4^\circ\text{C}$  at T1. The analysis of the data obtained after normalizing the temperature of exhaled air for the environmental temperature (nPLET) confirmed a similar significant reduction of values from  $8.46^\circ\text{C} \pm 0.42^\circ\text{C}$  at T0 to  $5.9^\circ\text{C} \pm 0.13^\circ\text{C}$  at T1 (*P* = .0001). The individual data for PLET and for eosinophil percentage in sputum samples are plotted in Fig 1.

The present study was ancillary to an investigation aimed to evaluate markers of airway inflammation in exhaled breath condensate and in induced sputum from asthmatic children living in an Alpine environment.<sup>9</sup> The finding of a reduction in exhaled cysteinyl leukotrienes and 8-isoprostane concentrations and a decrease in eosinophil airway inflammation after a 3-month stay in the mountain environment was consistent in a reduction of airway inflammation in the children participating in the study.<sup>9</sup> A striking finding in the present study was the reduction in the level of exhaled air temperature, which was observed under the same experimental conditions. At present, only 2 studies have been published measuring air temperature and asthma.<sup>9,10</sup> The results of the present study lend further support to the hypothesis that measurement of exhaled air temperature can serve as

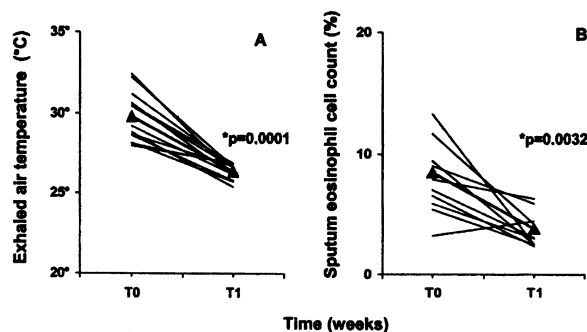


**FIG 1.** Values of exhaled air temperature ( $^\circ\text{C}$ ; **A**) and sputum eosinophil cell count (%; **B**) at baseline (T0) and after (T1) 3 months of antigen avoidance. \**P* < .05 compared with T0.  $\blacktriangle$ , Mean values.

a useful surrogate marker of airway inflammation in asthma.

In the present study the correlation of the simultaneous reduction in sputum eosinophil counts and exhaled air temperatures did not reach statistical significance, possibly because of the small sample size (type II error). However, the analysis of the relationship of intra-individual variations between exhaled air temperature and eosinophil content in sputum showed that all but one subject presented a correlated reduction of the 2 investigated parameters. Previous studies have shown significant correlations between exhaled markers of inflammation and values of exhaled air temperature in asthma.<sup>6,7</sup> Paredi et al<sup>6</sup> showed a more rapid increase in exhaled air temperature ( $\Delta e^\circ\text{T}$ ) in asthmatic patients in comparison with control subjects, with  $\Delta e^\circ\text{T}$  being positively correlated to exhaled NO (FeNO). Similarly, we observed a significant relationship between PLET and FeNO in a group of asthmatic children.<sup>7</sup> Although these 2 studies present seemingly different approaches to methods of calculation of a temperature-related parameter of airway inflammation (ie,  $\Delta e^\circ\text{T}$  and PLET), they both suggest that the exhaled air temperature in asthmatic patients is related to the degree of airway inflammation, possibly reflecting greater tissue hyperemia than normal, which is characteristic of inflammation.<sup>6</sup> In addition, it is possible that the inflammatory cells can contribute to the increase in exhaled air temperature because of the release of proinflammatory cytokines.<sup>10</sup>

This hypothesis, however, needs to be further explored to better characterize the relationship between tissue hyperemia, airway inflammation, and exhaled air temperature in asthma. In conclusion, the results of the present study further support the hypotheses that exhaled air temperature can reflect the level of airway inflammation in asthmatic children, thus providing a potentially useful noninvasive marker to monitor patients with asthma, particularly in pediatric populations.

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