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Can immunotherapy prevent progression to asthma in allergic individuals?

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To the Editor:

In their interesting and provocative article, Moller et al¹ demonstrate that allergen-specific immunotherapy (SIT) is effective in preventing progression to asthma in allergic individuals, thus supporting the view that SIT should be considered earlier in the treatment of rhinitis to prevent progression to more advanced and irreversible type of allergic diseases, such as asthma. Their findings are in agreement with our recent observations in a randomized, double-blind, placebo-controlled, parallel-group study of nonasthmatic subjects with seasonal allergic rhinitis.² By the end of this study, 47% of the subjects in the placebo group had asthma symptoms as opposed to only 14% of those in the SIT group. Moreover, in a large retrospective survey of nonasthmatic subjects with allergic rhinitis, we have reported that patients receiving immunotherapy have a 40% less chance of having asthma compared with untreated patients.³

Although the findings by Moller et al¹ clearly support the evidence that use of immunotherapy in nonasthmatic children with rhinitis can reduce their risk of asthma

development in the future, the ample variability in the results between study centers is of importance, deserves attention, and should have been discussed more in detail. Because bronchial hyperresponsiveness (BHR) might identify patients with rhinitis who are at risk for asthma progression,⁴ it would be important to verify whether the absence of prevention in asthma progression by SIT is associated with a lack of protective effect on methacholine BHR in the same centers.

The discrepant protective effects of SIT on the development of asthma between centers might be related also to the specific characteristics of the inhalant allergen type in that particular region or area. Recurrent exposure to allergens with strong allergenic properties might eventually dictate progression of the allergic march toward asthma, and a situation like this is less likely to be influenced by the protective effect of SIT. Therefore more information regarding the most representative inhalant allergen type associated with each center would have been important in providing an explanation for the observed variation between centers.

In addition, because it is possible that some sex-dependent reduction in asthma prevalence around the time of puberty occurs as a result of hormonal modifications,⁵ any important difference in terms of age or sex distribution in both treatment groups at each center might influence results and justify the variability between study centers.

It is not known why SIT should prevent progression to asthma in some allergic individuals, but one explanation rests in the potential of SIT to attenuate BHR and lower airway inflammation. In the study by Moller et al,¹ changes in BHR to methacholine appear to be negligible (well within the challenge repeatability of 1 doubling dilution), and I fear that nonparametric analysis is producing a statistically significant result that has trivial clinical importance: by the end of the study, PC₂₀ methacholine increased from 12.2 to 14.9 mg/mL for the control and SIT groups, respectively. We also failed to detect an important effect of SIT against BHR to inhaled methacholine (and sputum eosinophils) in nonasthmatic subjects with allergic rhinitis.² However, our data indicate that SIT can prevent seasonal deterioration of airway responsiveness to inhaled AMP. All participants in the placebo group became hyperresponsive to AMP (with 3 new patients having hyperresponsiveness to AMP), whereas no new cases of AMP hyperresponsiveness were observed in the SIT-treated group (one patient became hyporesponsive to AMP). Further analyses of this study revealed that low values of AMP PC₁₅ (but not methacholine PC₁₅) are good predictors of subsequent asthma progression in nonasthmatic subjects with allergic rhinitis. In addition, logistic regressions showed that AMP PC₁₅ is likely to forecast the prophylactic effects of SIT in preventing the natural course of the disease. Although larger studies are needed to define the characteristics of the patients who would benefit most from such a therapeutic approach, this observation indicates that BHR to inhaled AMP might be useful to identify those in whom SIT might be effective at preventing progression to asthma.

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TOP

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