

moderately complex assay that was originally introduced by MAST Immunosystems in 1983. It is a laboratory-based screening test that measures IgE antibody to a panel of allergens. Serum is drawn into the pipette device, and IgE antibody, if present, binds to allergen immobilized on threads and then is detected with labeled anti-IgE. Because it is an established semiquantitative screening assay that requires performance in the laboratory, it along with the Thabest IgE test (Molecular Medicine Inc, Denville, NJ) was not overviewed within the context of the article, which focused primarily on quantitative assays. There was, however, no intent to exclude any technology, and thus for completeness, both the CLA Allergy Test and the Thabest IgE Test should have been mentioned as a counterpoint to the ImmunoCAP Rapid (Phadia, Uppsala, Sweden). One strength of the CLA Allergy Test over the current ImmunoCAP Rapid is the availability of IgE antibody measurements to a greater number of allergen specificities. The ImmunoCAP Rapid, however, was singled out in this article because it is the first assay that involves the use of a finger prick sample of blood and a reader that can be used by a non-laboratory-trained individual. As such, it has been positioned as a technology that can be performed by unskilled employees in a primary health care office or a patient's home. This contrasts with the CLA Allergy test and Thabest IgE Test, which both require performance in a clinical laboratory. We thank Dr Saper for expanding the focus of our article to ensure mention of all the semiquantitative IgE antibody assays used in North America.

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Lack of pretreatment cost-effectiveness and side effects of omalizumab versus prednisone/montelukast on tolerability of immunotherapy

To the Editor:

The article "Effect of pretreatment with omalizumab on the tolerability of immunotherapy in allergic asthma"¹ left me troubled, in that there was no editorial comment or any letters to the Editor commenting on the cost or the extensive time (13 weeks) required for pretreatment in those patients not controlled on inhaled corticosteroids for immunotherapy to be carried out. The addition of montelukast and/or a brief course of prednisone is frequently effective and is much less costly, and immunotherapy can be carried out much, much sooner.

Regretfully, cost, side effects and pretreatment duration with omalizumab were never addressed in relation to the alternatives.

J. Loren Rosenberg, MD

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Reply

To the Editor:

Dr Rosenberg¹ questions the cost effectiveness of omalizumab as a pretreatment for immunotherapy compared with prednisone and/or montelukast. The objective of our study was to determine whether pretreatment with omalizumab was safe and effective in terms of reducing the likelihood of systemic allergic reactions associated with initiating specific allergen immunotherapy in a population considered to be at high risk for adverse events. An analysis of costs was not an objective of the study. Although the question of cost is important to consider, in this complex situation there would be multiple factors to evaluate. Besides the costs of omalizumab pretreatment and allergen immunotherapy, there would be the costs avoided such as those associated with treating systemic allergic reactions and asthma exacerbations and the benefits of achieving maintenance immunotherapy. Dr Rosenberg¹ mentions the use of possible alternatives such as montelukast or a brief course of prednisone. Indeed, many studies have evaluated different premedication regimens for various types of immunotherapy using rush, cluster, and conventional dosing. However, neither of these agents has been evaluated according to the objectives of our study, particularly in patients with moderate-severe allergic asthma experiencing persistent symptoms despite use of inhaled corticosteroids. In fact, 35% of patients were pretreated with antihistamines in our study. *Post hoc* analysis showed that antihistamine pretreatment had no effect on the number of systemic allergic reactions. Not surprising, the majority of our study patients experienced respiratory grade 3 systemic allergic reactions. Omalizumab had a pronounced effect on reducing these events (6 with omalizumab pretreatment vs 24 with placebo). The potential benefits of montelukast or a short course of prednisone in terms of both reducing systemic allergic reactions and improving asthma control in this population are yet to be demonstrated in the context of appropriately designed clinical trials. In contrast, these benefits were demonstrated by omalizumab in our trial and enabled more patients to tolerate initiating immunotherapy and to achieve the target maintenance dose.

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Merck; and receives research support from the NIH-NIAID, the NIH-NHLBI, Novartis, AstraZeneca, GlaxoSmithKline, MedImmune, and Ception.

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Forced expiratory flow between 25% and 75% of vital capacity may be a marker of bronchial impairment in allergic rhinitis

To the Editor:

Simon et al¹ have published a very interesting study conducted in a cohort of children with asthma. These authors suggest that forced expiratory flow between 25% and 75% of vital capacity (FEF₂₅₋₇₅) should be considered in children with asthma and normal FEV₁ and might predict the presence of reversible airflow obstruction. We agree with them that the usefulness of FEF₂₅₋₇₅ should be re-evaluated. Moreover, the editorial by McFadden² pointed out that long-term studies will be required to reach definitive conclusions about the ultimate clinical utility of FEF₂₅₋₇₅ in asthma management.

However, we would like to highlight the further role of FEF₂₅₋₇₅ as a diagnostic and prognostic marker of bronchial involvement in patients with allergic rhinitis (AR). This issue is strongly supported by the concept of a tight connection between AR and asthma, underlined by the American guidelines on rhinitis³ and the Allergic Rhinitis and its Impact on Asthma document.⁴ The first document states that a reduced FEF₂₅₋₇₅ may be considered a marker of early bronchial pathology in patients with AR.³ The latter document, addressing the association between AR and asthma,⁴ suggests that FEV₁ may not be sensitive enough to detect small airways obstruction in some patients with rhinitis, quoting 2 recent articles on FEF₂₅₋₇₅ in which this parameter was identified as predictor of early bronchial involvement in this patient population.^{5,6} More recently, it has been reported that an initial bronchial airflow obstruction, detected by impaired FEF₂₅₋₇₅ values, occurs in 23% of a large cohort of patients with a recent onset of AR and normal FEV₁ values.⁷

To evaluate this topic further, we conducted a preliminary analysis in young adults with AR to define a cutoff value of FEV₁ for identifying overt impaired FEF₂₅₋₇₅ values (such as <65% of predicted). This cross-sectional study included 4782 subjects (71% males; mean age, 25.4 years) with AR but no current or past asthma symptoms.

Medians and percentiles (25th and 75th) were used as descriptive statistics. A receiver operating characteristic curve analysis was performed to determine a cutoff for FEV₁ that could optimize the sensitivity and the specificity of the test to identify patients with a FEF₂₅₋₇₅ value >65%. Medcalc 9 (Milan, Italy) was used for computation.

The median FEV₁ value was 91% (25th, 83%; 75th, 96%), the median forced vital capacity value was 100% (25th, 90%; 75th, 104%), and the median FEF₂₅₋₇₅ value was 72% (25th, 66%; 75th, 75%); 3691 patients (77%) showed a FEF₂₅₋₇₅ value >65% of predicted normal values. By receiver operating characteristic analysis, we were able to show a FEV₁ value >85% to be

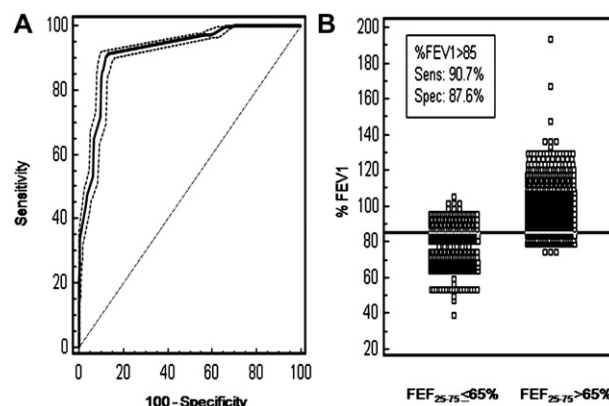


FIG 1. Receiver operating characteristic curve (A) and discrimination ability of the chosen cutoff of 85% for the FEV₁ values in patients with FEF₂₅₋₇₅ ≤65% and FEF₂₅₋₇₅ >65% (B). Sens, Sensitivity; Spec, specificity.

the optimal cutoff to discriminate patients with FEF₂₅₋₇₅ >65%. The associated sensitivity and specificity were 90.7% (95% CI, 89.7-91.6) and 87.6% (95% CI, 85.5-89.5), respectively. The positive and negative predictive values were 96.1% and 73.6%. The corresponding area under the receiver operating characteristic curve of 0.92 (95% CI, 0.91-0.93) indicated a good discriminating ability (Fig 1).

Therefore, an FEV₁ value still in the lower part of the normal range, such as higher than 80% of predicted as stated by the Global Initiative for Asthma guidelines (<http://www.ginasthma.com>) could be associated in patients with AR with overt reduction of forced expiratory flows. In conclusion, FEF₂₅₋₇₅ should be carefully assessed in patients with AR.

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