IgE Sensitization to *Aspergillus fumigatus* Is Not a Bystander Phenomenon in Cystic Fibrosis Lung Disease

To the Editor:

We have read with great interest the article by Baxter et al\(^1\) in CHEST (May 2013) highlighting the importance of sensitization to *Aspergillus fumigatus* (Af) in progression of cystic fibrosis (CF) lung disease. We and many others have previously reported that sensitization to Af is frequent in patients with CF: It was observed in 31% of the patient cohort (n = 153) who were followed up at the Leuven CF referral center.\(^2\) We also confirmed significantly impaired lung function parameters in Af-sensitized compared with Af-nonsensitized patients, with an average difference in FEV\(_1\) of 19 ± 4% predicted. In a multivariate analysis with age, sex, BMI, *Pseudomonas aeruginosa* colonization, pancreatic insufficiency, and gastroesophageal reflux disease as covariates, a significantly lower FEV\(_1\) and vital capacity (P < .001) was associated with Af sensitization, as well as an increased airway resistance (P < .05) and hyperinflation (higher residual volume, P < .001) (e-Table 1). Interestingly, no significant differences in lung function parameters were found between patients with serologic criteria for allergic bronchopulmonary aspergillosis (ABPA) (n = 17) and patients with sensitization to Af without ABPA. Similar to the data presented by Baxter et al\(^1\) and others,\(^3\) we observed, in a 3-year period, more exacerbations in Af-sensitized patients with CF compared with patients without sensitization to Af (5.30 ± 4.54 vs 1.69 ± 2.78 hospital admissions for IV antibiotic therapy, respectively; P < .005).

The group of Baxter and Dunn has recently proposed a novel classification of *Aspergillus* disease in patients with CF.\(^4\) However, interesting from a pathophysiologic point of view and to guide further therapeutic trials, our data on pulmonary function and exacerbation rate show significant differences only for Af-sensitized vs nonsensitized patients. If we reclassified the nonsensitized patients in two groups taking into account the absence or presence of Af IgG, no significant differences were seen between “nondiseased” and “Af-bronchitis” patients.

To date, most evidence has, thus, emerged for the role of Af sensitization, which raises the question if treatment of Af-sensitized patients, even before ABPA is present, could result in better outcomes. The rationale would be to lower Af allergic burden and/or to inhibit the resulting hypersensitivity response, before pulmonary function decline or ABPA develop. Whether such a treatment should consist of antifungal therapy, as in the pivotal Fungal Asthma Sensitization Trial (FAST) in severe asthma\(^5\) or should aim to prevent the IgE-mediated hypersensitivity remains to be elucidated. A placebo-controlled intervention study evaluating monitored antifungal treatment (itraconazole, voriconazole), early treatment with anti-IgE therapies such as omalizumab, or perhaps a combination of both seems indicated in Af-sensitized patients with CF.

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Additional information: The e-Table can be found in the Supplemental Materials section of the online article.

References

1. Baxter CG, Moore CB, Jones AM, Webb AK, Denning DW. IgE-mediated immune responses and airway detection of *Aspergillus*...


