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Will the Real Risk Factor for Airway Disease Please Stand Up?

Over the past decade, many investigators have been intrigued by the possibility that cigarette smoke interacts with the immediate hypersensitivity immune system to cause lower respiratory tract bronchoplastic disease.1-3 The quantitative immunoglobulin (Ig) E level is considered to be a nonspecific monitor of the activity of the immediate-type hypersensitivity immune system. Skin reactivity to prick tests is considered to be a more specific indicator of the activity of this system. Similarly, routine FEV1 studies can nonspecifically reflect respiratory tract diseases, whereas bronchoprovocation with methacholine or histamine is a more sensitive indicator of airway dysfunction. Smoking habits can be described as “current,” “non-,” “ex-,” or “passive.” Analysis of patients with use of the above parameters has raised many provocative ideas regarding the importance of IgE, either specifically or nonspecifically, in the eventual decline of lung function.4

In this issue of Chest (see page 642), a team of French investigators reports its analysis of the data on 310 adult men in regard to IgE level, skin prick tests, FEV1, studies, response to inhaled methacholine, and smoking habits; all parameters were again measured five years later. An elevated IgE level (greater than 100 IU/ml) was noted in 29 percent of these men and correlated with reactivity of prick tests and symptomatic asthma. This finding would not be unexpected. In fact, Gergen and Turkeltaub recently confirmed the increased prevalence of asthma with positive allergen skin tests in nonsmokers, thus implicating atopy as a predisposing condition for symptomatic airway disease.

A new and more surprising finding in this study was the subgroup of patients who demonstrated a significantly more rapid decline in FEV1. These patients had elevated IgE levels and were nonsmokers but did not demonstrate atopy by either skin reactivity or symptomatic asthma. A similar correlation was also noted in the ex-smokers.

These results now stimulate further inquiries as to the interaction of IgE with the lower airway. If the IgE is not responding to aeroallergens, then perhaps it is reacting to something else which may eventually cause respiratory dysfunction. Vehicular traffic exposure, chronic infection (phlegm), extrinsic allergens, and even alcohol consumption could not be correlated with IgE level in this study. Perhaps α1-antitrypsin phenotypes should have been examined in order to detect any genetic predisposition to airway disease.

One type of smoking category not addressed in this study was “passive smoking.” The literature abounds with various studies on the effect of secondhand smoke on airway function.6,7 Even prenatal exposure to smoke can raise the IgE level in cord blood.8 Elevated IgE levels in children of smoking parents have been documented and found to correlate with increased respiratory symptoms in children.9 Perhaps the French men studied had exposure to secondhand smoke at work or at home, thereby increasing their risk for lung disease.

The authors also postulate that an elevated IgE level may lead a patient to develop or continue a smoking habit. There is a lack of substantiating data for this statement, especially because initial IgE samples on the patients studied were accidentally lost.

Whatever the explanation for the rapid decline in FEV1 in these subjects, it would be best to refrain from overinterpreting the importance of these data. The nonsmoking male patient with an elevated IgE level should not feel “doomed” to develop lower airway disease without more corroborative evidence. Also, reanalysis of these patients in another five years may demonstrate a shift in data, whereby smokers with elevated IgE levels would have the lowest FEV1 values, but nonsmokers’ function would have improved or remained the same. Continued study of this group will be of great interest.

In conclusion, the real risk factor (if there is one) for lower airway disease remains elusive. However, further studies, such as the one in this issue, may
perhaps unravel the mystery in years to come.

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Isolated Systolic Hypertension
New Management

Isolated systolic hypertension (ISH) has been recognized as a finding primarily in older subjects. About 3 million Americans aged 60 and older have an elevated systolic blood pressure, and this is expected to increase to 8 million by the year 2025. This condition increases with age (22 percent of those older than 80). It is associated with a two to three times higher risk of stroke and increased risk of coronary heart disease, congestive heart failure, and sudden death. Isolated systolic hypertension is defined as persistent elevation of systolic blood pressure to 160 mm Hg or higher and diastolic pressure of ≤90 mm Hg. While the benefits of treating diastolic hypertension have been established, the benefit of treating ISH had been unproved.

To answer the question whether there is benefit in lowering the pressure in ISH, the Systolic Hypertension in the Elderly Program (SHEP) study was designed as a multicenter trial. The results were published in June 1991 and indicate that elderly subjects could be enrolled and that they benefited from a simple, relatively inexpensive antihypertensive program, which was well tolerated.

Men and women were recruited into a placebo-controlled, double-blind, stepped-care treatment program and were followed up an average of 4.5 years. Screening of 447,921 multiethnic persons aged >60 years yielded 4,736 (1.06 percent) subjects for the trial. Their mean age was 72; 57 percent were female; and 14 percent were black. Their mean blood pressure was 170/77 mm Hg at the outset.

The step-care medication regimen began with a diuretic, chlorthalidone, at two dosage levels (12.5 mg, 25 mg). Step two was a beta-blocker, atenolol, at two dosage levels (25 mg, 50 mg). Reserpine could be substituted for atenolol if the latter was not well tolerated. Ninety percent of the active-treatment group were receiving treatment at year 5; 48 percent were receiving diuretic alone.

The placebo group was managed in the community. At the close of the study, 44 percent had been placed on an antihypertensive regimen for various reasons by their doctors.

The primary objective was to determine whether long-term antihypertensive therapy reduced the occurrence of stroke. A secondary objective concerned the effects of treatment on other cardiovascular disorders, on dementia and depression, and on the possible adverse effects of long-term drug therapy. Two subgroup questions were addressed: About one third of the participants had been receiving drug therapy that was withdrawn prior to entering the treatment program; would their results differ from those in the remainder? Would participants with resting ECG abnormalities (61 percent of participants) fare differently from those with a normal ECG? The goals of treatment were as follows: if baseline systolic pressure was ≥180 mm Hg, to lower it to <160 mm Hg; if baseline systolic pressure was ≥160 to 179 mm Hg, to reduce pressure by at least 20 mm Hg.

Throughout the trial, the mean systolic blood pressure of the active-treatment group was lower than the initial blood pressure by about 26 mm Hg. The mean diastolic pressure was lower by about 9 mm Hg. For the placebo group, the systolic pressure was 15 mm Hg lower, and the diastolic was 4 to 5 mm Hg lower. At five years, the mean pressure for the active-treatment group was 144/68 mm Hg, compared with 155/71 mm Hg for the placebo group. During the trial, goal blood pressure was reached by 65 percent to 72 percent of the active-treatment group and by 32 percent to 40 percent of the placebo group.

During the mean follow-up period of 4.5 years, there were 103 persons with stroke in the active-treatment...