Two recently published articles in the Journal have provided further evidence to support the notion that prior histories of inflammatory- and/or allergy-related diseases are inversely associated with lung cancer risk. In a large prospective cohort study of over 1.1 million US men and women, Turner et al. (1) reported significant inverse associations between a history of both asthma and hay fever (relative risk (RR) = 0.73, 95 percent confidence interval (CI): 0.65, 0.83) or just hay fever alone (RR = 0.85, 95 percent CI: 0.80, 0.90) and lung cancer mortality. Subsequently, in a large case-control study comprising 2,854 cases and 3,116 controls from seven different European countries, Castaing et al. (2) noted that history of eczema was inversely associated with lung cancer risk (odds ratio (OR) = 0.61, 95 percent CI: 0.48, 0.76).

The data from Turner et al. (1) confirm our own previously published findings (3) that self-reported, physician-diagnosed hay fever is inversely associated with lung cancer risk (OR = 0.55, 95 percent CI: 0.48, 0.70), and this pattern was evident in both ever and never smokers, even after exclusion of diagnoses made up to 10 years before interview. Additionally, Castaing et al. (2) reported an inverse association between a history of eczema and lung cancer risk for never smokers (OR = 0.55, 95 percent CI: 0.28, 1.08). However, Turner et al. reported no association between hay fever and lung cancer mortality in never smokers (RR = 1.02, 95 percent CI: 0.86, 1.21) and a nonsignificant inverse association for persons with both asthma and hay fever (RR = 0.83, 95 percent CI: 0.56, 1.22). Thus, the authors suggest that the inverse associations in the overall population were likely due to residual confounding by smoking or self-selection bias associated with smoking behavior. By comparison, in our subsequent analyses (4) restricted to lifetime never smokers (n = 280 cases), we found increased risks (1.9-fold for women and 4.4-fold for men) for a history of both asthma and hay fever. But, because of a small sample size of never smokers, the odds ratios were not statistically significant.

As we (3) and Turner et al. (1) previously hypothesized, an unmeasured exposure, such as allergy medications, may in part explain the inverse association between allergy-related disease and lung cancer. There are several classes of over-the-counter and prescription allergy medications, including antihistamines, decongestants, corticosteroids, bronchodilators, mast cell stabilizers, and leukotriene modifiers. They block allergy symptoms through various mechanisms; however, their role in lung cancer carcinogenesis is unclear. Yet, because persons with a history of allergy may self-selectively reduce or completely avoid certain environmental exposures and allergy triggers (e.g., secondhand smoke, occupational carcinogens, air pollution, or dietary constituents) (2), these factors must be accounted for and explored in depth in subsequent studies. It is also plausible that the reduced risks may be due to the “immunesurveillance hypothesis” by which a stimulated and/or enhanced immune system is more efficient in detecting and destroying malignant cells.

In summary, the empirical evidence to support an inverse association between allergies and lung cancer has been largely derived from observational epidemiologic data. Additional research is warranted to confirm this association, including a thorough assessment of history of allergy medication use, putative allergy triggers, and frequencies of biologically relevant, pathway-specific single nucleotide polymorphisms. More importantly, the biologic mechanism(s) for the role of history of allergy and lung cancer needs to be studied, with specific attention to inflammatory and immune response, a recommendation that was put forward by the National Cancer Institute’s Lung Cancer Progress Review Group in 2001 (5).
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REFERENCES


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Editor’s note: In accordance with Journal policy, Turner et al. and Castaing et al. were asked whether they wanted to respond to this letter. The response by Turner et al. follows; Castaing et al. chose not to respond.

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