

THE AUTHORS REPLY: In our paper we reported that G446A has a statistically significant association with the risk of familial cancer, as compared with sporadic cancer; we did not find a differential frequency when we compared sporadic cancers with healthy controls. Further independent studies reported statistically significant associations of Trp149Stop and Cys148Arg with the risk of familial breast cancer.^{1,2} For these reasons, it is quite surprising to us that Sellick et al. report their results in all patients with CLL without considering the family history. It would be interesting to see the odds ratio calculated from their data after stratification by family history. Also, it would be of interest to know if there were any cases among their patients who had CLL with ARLTS1 (Trp149Stop variant) of familial CLL with evidence of segregation of the malignant phenotype along with the genetic abnormality, as was

the case in the CLL family we reported. In our article, we stated, “we propose that ARLTS1 is a low-penetrance tumor-suppressor gene that accounts for a small percentage of familial melanoma or familial CLL.” In light of the multigenic predisposition to familial CLL, the letter from Sellick et al. does not negate this hypothesis.

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Allergic Rhinitis

TO THE EDITOR: Drs. Plaut and Valentine (Nov. 3 issue)¹ did not mention the use of saline nasal irrigation for the patient with seasonal allergic rhinitis. The student described in the case vignette wanted to avoid drowsiness and dry mouth. Nasal irrigation makes symptoms more tolerable and is an excellent addition to nasal corticosteroids.²⁻⁴

At the very least, it helps reduce the mucus to which the nasal inhaled steroids adhere. A controlled trial showed a significant improvement in symptoms.²

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TO THE EDITOR: Plaut and Valentine indicated that the sensitivity and specificity of in vitro tests

for serum IgE antibody to allergens are equal to that of skin testing. The sensitivity and specificity of in vitro serology differ for various allergens and are not equivalent to skin-test methods.¹ Food allergens have been most comprehensively studied to determine the clinical sensitivity of tests for specific IgE antibodies, and IgE thresholds have been determined that define 95 percent probability of a negative challenge.² However, equivalent decision levels with such clinical predictions are not available for outdoor aeroallergens, and there are no studies that directly compare diagnostic equivalence of in vitro testing with that of in vivo testing.³ The immediate hypersensitivity test by the skin-prick method with wheal and flare measurement still is the gold standard for diagnosis of IgE-mediated aeroallergen allergy because of its unparalleled sensitivity.¹ Thus, testing for serum IgE antibody and the immediate hypersensitivity skin test are both acceptable for determining respiratory allergies, but they are not equivalent.⁴

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THE AUTHORS REPLY: Dr. Boiko advocates the use of saline nasal irrigation. Although saline may be useful as a palliative treatment in allergic rhinitis,¹ it is used more commonly in nonallergic rhinitis (bacterial rhinitis and vasomotor rhinitis).² Since its effect as an active intervention might be indistinguishable from that of placebo, we chose not to include saline in our list of pharmacologic agents.

Drs. Noroski and Davis raise the question of whether in vitro tests for serum IgE antibody are as sensitive and specific as skin testing. They have accurately noted that more data would be useful to provide a clearer comparison of the sensitivities of in vivo and in vitro assays with respect to outdoor aeroallergens. It is important to note that both in vivo assays (typically skin-prick tests) and in vitro assays have sufficient sensitivity to provide comparably useful clinical information for allergic rhinitis. The two main approaches to allergen skin testing are by the prick and intradermal routes. Intradermal testing has greater sensitivity but lower specificity than prick testing, and thus does not appear to be more clinically useful in allergic rhinitis than prick or in vitro testing. Skin-prick testing is moderately more sensitive but less specific than radioallergosor-

bent testing. More recently, newer variants of the radioallergosorbent test and the enzyme-linked immunosorbent assay have been developed that are more sensitive than the original radioallergosorbent test. These newer in vitro tests are only slightly less sensitive than skin tests,³ and their specificity may be greater.⁴ Thus, if either one or the other type of test has the advantage, it may result from lower cost or greater convenience, rather than sensitivity or specificity.

We also wish to clarify a statement in our original article. The use of a semicolon before the comment "increased intraocular pressure and posterior subcapsular cataracts have been reported in adults" may have inadvertently suggested that these complications have been reported only with intranasal beclomethasone, whereas they also have been reported with other nasal corticosteroids.

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Safety of Long-Acting Beta-Agonists

TO THE EDITOR: The recommendation in the Perspective article by Martinez (Dec. 22 issue)¹ of adding leukotriene modifiers or theophylline to therapy for asthma that is not controlled with the use of inhaled corticosteroids is completely opposite to that of the National Asthma Education and Prevention Program expert panel, which prefers the addition of long-acting beta-agonists.² A Cochrane review showed that adding long-acting

beta-agonists, instead of leukotriene modifiers, to the treatment of asthma not controlled by inhaled corticosteroids would prevent one exacerbation for every 38 patients treated.³ If only 25 percent (thought to be a large underestimate⁴) of the 19 million Americans with asthma⁵ have moderate-to-severe disease, then Martinez's recommendation would result in 125,000 excess exacerbations. No study has shown that the combination