Prevention and Treatment of Glucocorticoid-induced Osteoporosis

To the Editor:

We read with interest the article by Libanati and Baylink,1 which appeared in the November 1992 issue of Chest. We hope to see more articles addressing this topic in the future. The topic of glucocorticoid-induced osteoporosis should be important to every physician treating bronchial asthma because the 1991 report of the National Heart, Lung, and Blood Institute on asthma emphasizes the use of anti-inflammatory medications. As care for asthmatic patients changes, an increasing number of patients will be given prescriptions for an inhaled corticosteroid. Patients who only inhale steroids or who take short courses of oral steroids have increased bone turnover, decreased bone formation, and reduced vertebral bone density.2,3 As Libanati and Baylink noted, there are no long-term data. The longest average duration on inhaled corticosteroids was 3 years.4 Whether prophylaxis for osteoporosis should be a standard part of care for these patients has not been addressed, and it should be.

As physicians consider the preventable problem of glucocorticoid-induced osteoporosis, we would like to suggest and emphasize several alternatives that may decrease the incidence in the future: (1) steroid-sparing drugs,5 (2) etidronate,6 and (3) pamidronate.7 We agree with Libanati and Baylink that patients receiving corticosteroids should have a baseline measurement of bone density, preferably by means of dual-photon absorptiometry.8

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Pectin-induced Occupational Asthma

To the Editor:

We read with great interest in the November 1992 issue of Chest the report of pectin-induced occupational asthma by Kraut et al.4 Because pectin-specific IgG4, not IgE, was identified in the patient's serum, the authors conclude that this case of asthma was IgG4, not IgE, mediated. We propose that in fact the data presented are in favor of an IgE-mediated cause and offer explanations for the serologic results obtained.

IgG4-mediated human basophil activation has been described;2
however, attempts to localize IgG4 to the surface of mast cells or basophils have been unfruitful. These cells possess only Fc receptors specific for IgE and not IgG. Furthermore, antigen-specific IgG4 is thought to play a protective, rather than a detrimental, role, arising after successful immunotherapy. For these and other reasons, convincing evidence for an IgG4 reagin is lacking.

In the patient described, a prick test evoked an immediate wheal and flare response, and pectin inhalation challenge induced immediate bronchospasm—strong evidence for an IgE-mediated type 1 hypersensitivity to pectin. An IgG4+, rather than IgE-, mediated etiology is proposed due to the failure of isolation of pectin-specific IgE by enzyme-linked immunosorbent assay (ELISA); however, without a positive pectin-specific IgE ELISA control, the sensitivity of the test is in question. Even with a sensitive IgE pectin-specific ELISA, nanograms of pectin-specific IgE might well go undetected in the presence of milligrams of pectin-specific IgG4, due to competitive inhibition. Adequate adsorption of IgG from the patient’s serum prior to performing the pectin-specific IgE ELISA is required before proclaiming the patient’s serum devoid of pectin-specific IgE. Finally, without serum measurement of pectin-specific IgG4 from a pectin-exposed non-asthmatic coworker control, the pathogenic importance of the patient’s pectin-specific IgG4 is at best, speculative.

In conclusion, although the finding of pectin-specific IgG4 in this patient’s serum is interesting, we differ with the authors’ conclusion that it is pathogenic. We believe, rather, that the data suggest an IgE-mediated type 1 hypersensitivity to pectin.

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To the Editor:

Drs. Baldwin and Shah feel that our recent report of pectin-associated asthma is more in keeping with an IgE-mediated hypersensitivity reaction than with an IgG4 mechanism, as we postulated. Specifically, they question the sensitivity of our IgE ELISA and raise the possibility that because of competitive inhibition by pectin-specific IgG4, we were unable to detect minute amounts of pectin-specific IgE.

In a previous study of patients receiving long-term immunotherapy, ragweed-specific IgE could still be measured in our laboratory in the serum samples of individuals with high ragweed-specific IgG4 and IgG1. Since similar methodology was used in this study, we believe that the negative pectin IgE analysis is accurate. We agree that having a pectin-specific IgE positive control would have been useful. As descriptions of pectin allergy, however, are currently still at the case report level, to our knowledge no such control exists.

Although IgE is responsible for type I hypersensitivity and is closely associated with allergy, some clinical problems are not well explained by either the presence or the level of total or specific serum IgE. For example, recent work has shown that antigen-specific IgE does not play a significant role in western red cedar asthma, suggesting that other mechanisms must be causal.

The role of IgG4 in allergy is controversial. Although IgG4 has been reported to play a protective role in some studies, negative correlations between IgG4 response and clinical improvement were found in two Danish studies of grass and Cladosporium immunotherapy. A good prognosis was correlated with a low specific IgG4 titer in a study of individuals with dust-mite allergy.

Our current data suggest that IgG4 may have caused the asthmatic response. Had the individual returned for follow-up, we would have attempted to confirm our impression by passive sensitization of basophils with the patient’s serum before and after depletion of IgG. Then, basophils would have been challenged by pectin in different concentrations and histamine release measured.

Our data provide a clue to one of the possible mechanisms of allergy—IgG4-mediated sensitization. It should be noted that in another case of pectin-associated asthma IgG, not IgE, antibodies were detected. In this study, the IgG subclass was not documented. Although positive skin and bronchial responses usually suggest an IgE-mediated hypersensitivity, in cases in which serum-specific IgE is not detected, other possible pathogenetic mechanisms should be considered, the most likely in this case being the increased pectin-specific IgG4.

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Rib Biopsy

To the Editor:

In an article that appeared in the October 1992 issue of Chest, Dr. Ikard1 stresses that accurate preoperative chest wall localization of the lesion prior to open rib biopsy is crucial. The intraoperative finding of normal-appearing ribs poses perplexing problems to the surgeon, and extralobar biopsies are not uncommon.

We would like to describe the method that we use in cases of discrete rib lesions that are not expected to cause gross rib deformity: The osteolytic lesion is localized preoperatively under radiologic guidance. The skin overlying the lesion is marked with a pencil to indicate the site of incision. A 21-gauge needle is brought