

Because at least a third of health care workers who develop latex allergy are atopic,¹ it is surprising that none of their subjects were. Given the current status of our knowledge of the long-term effects of latex allergy, I believe that much more investigation needs to be done before one can be certain that it could lead to "permanent disability."

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Reply

To the Editor:

Dr. Leynadier makes a very interesting comment. Did our article (*J Allergy Clin Immunol* 1995;96:457-64) demonstrate that latex allergy may lead to permanent disability, even if latex exposure has been eliminated, or instead, were the subjects still exposed to low concentrations of latex? Natural rubber is ubiquitous, and latex allergens have been found in medical settings where latex gloves are never or seldom used¹ and in the city environment.² Nevertheless, low concentrations of latex have yet to be demonstrated to cause asthmatic attacks in sensitized subjects. On the contrary, Vandenplas et al.³ showed that reduced (not absent) concentrations of latex in the work environment significantly improve bronchial responses of subjects with latex-induced asthma. Moreover, our hypothesis of permanent disability in subjects 1, 2, and 3 is supported by the fact that asthmatic symptoms were not work-related and were associated with bronchial hyperresponsiveness and significant variability in peak expiratory flow.

Dr. Leynadier is surprised that four of six subjects experienced a late asthmatic response to an inhalation provocation test and asks whether symptoms could be related to allergens other than latex. Because all subjects have been demonstrated to be allergic to latex and had a positive response to an inhalation provocation test with latex, we do not have any reason to suppose that two thirds of our subjects were allergic to other unknown allergens. Moreover, late asthmatic responses are very common in professional settings.⁴

We could not draw any conclusion about the relation between atopy and latex allergy because of small numbers; our results are in line with the frequency of atopy

in our area (about 20%).⁵ Further studies are needed to confirm our results.

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Agonizing over long-acting β -agonists

To the Editor:

If asthma represents a triad of airway inflammation, bronchial hyperreactivity, and airway constriction, then the introduction of long-acting β -agonists into the asthma pharmacopeia raises concerns. Regular use of β -agonists has been shown to increase sensitivity to nonspecific and allergen challenges and increase the late-phase response.^{1,2} There is also evidence suggesting that even short-term use of long-acting β -agonists may cause downregulation of β -receptors and/or increase bronchial hyperreactivity.^{3,4} These deleterious changes may only affect a subset of patients with asthma, but risk groups are not defined.

There is also a growing body of evidence that inflammation, late-phase reaction, and bronchial hyperreactivity may be uncoupled from one another. Further, ongoing inflammation can lead to permanent airway damage. Classic symptoms of asthma, especially nocturnal symptoms, need not represent a continuum of these perhaps distinct pathophysiologic mechanisms. Further, long-acting β -agonists mask time-held markers of asthma

control—symptoms and medication use. Thus if symptoms do occur, what significance do they merit? As well, because the duration of bronchodilation of long-acting β -agonists, such as salmeterol, is variable and often exceeds 12 hours, peak flow data may be misleading.

With the advent of long-acting β -agonists, the playing field has radically changed for the diagnosis and management of asthma. Aside from remaining questions of increased morbidity and mortality with use of long-acting β -agonists in select subpopulations, published guidelines concerning asthma management are lacking in their interpretation of the status of the asthmatic patient regarding severity, inflammation, and reactivity when short-acting β -agonists are required or when nocturnal symptoms occur in the setting of daily use of long-acting β -agonists.

Therefore in regard to long-acting β -agonist, we recommend the following:

1. Infrequent use as a prophylactic agent of exercise-induced asthma. Tolerance with routine use of salmeterol remains possible.⁵
2. Elucidation of the clinical implications of purported antiinflammatory effects.
3. Optimal inhaled antiinflammatory agents should be a criterion for the initiation of long-acting β_2 -agonists.
4. Periodic withdrawal of long-acting β_2 agents and subsequent monitoring of medication and symptom scores, peak flow measurements, or pulmonary functions.
5. Further studies establishing safety in the subpopulation of patients with severe asthma.
6. New guidelines delineating criteria for classification of patients with asthma taking long-acting β -agonists

and interpretation of symptoms, medication use, and peak flow measurements in the setting of their use.

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Editor's note: This issue also contains a detailed statement from the AAAAI Committee on Drugs on the same matter.

Correction

The following corrections apply to the article by Schwiebert et al., entitled "Glucocorticosteroid inhibition of cytokine production: Relevance to antiallergic actions," which was published in volume 97, pp. 143-52, 1996, of *The Journal of Allergy and Clinical Immunology*.

The first author's name should read: Lisa M. Schwiebert, PhD.

The abbreviation AP-1 stands for activator protein-1 (pp. 145, 146).

The abbreviation RANTES stands for regulated on activation normal T cell expressed and [presumably] secreted (p. 147).