

is true, it is also important to realize that "how effective" is not part of FDA criteria. A drug company only has to prove that their product is better than nothing (placebo).

In addition, he does not follow our reasoning regarding the relationship between plasma level of cromolyn, amount of drug delivered to the lungs, and clinical efficacy. The studies cited in our article³⁻⁷ clearly demonstrate a relationship between area under the cromolyn plasma concentration time curve (AUC) and dose of drug administered and adequacy of administration technique. Moreover, there is a strong correlation between AUC and long-term efficacy, as well as AUC and blocking of exercise-induced bronchospasm. The MDI available in the United States produces a much smaller cromolyn AUC and incompletely blocked the late phase and allergen-induced airway responsiveness in our study. In contrast, the 5 mg/puff MDIs available in Europe or the Spincaps have a much larger AUC and completely inhibit airway responses to allergen. Thus it is logical to conclude that the MDI currently available in the United States delivers less drug to the lungs than other formulations.

Lastly, Dr. Selcow points out that over the last 13 years, since they have switched from using theophylline to cromolyn and inhaled steroids, he has seen a remarkable reduction in emergency department visits and hospitalizations. It is difficult to understand how this could be because both children and adults are less likely to be adherent with cromolyn than with theophylline.⁸

Leslie Hendeles, PharmD
University of Florida
Health Science Center
P.O. Box 100486
Gainesville, FL 32610-0486
Eloise M. Harman, MD
University of Florida, Gainesville
David Huang, MD
Tallahassee Pulmonary Clinic
Ralph O'Brien, PhD
Cleveland Clinic Foundation
Cleveland, OH
Kathryn Blake, PharmD
Nemours Children's Clinic
Jacksonville, FL
Jeffrey Delafuente, MS
University of Florida, Gainesville

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1/8/66673

Comments on the 1995 Presidential address

To the Editor:

I have finished reading the Presidential address in the April issue of *THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY* (1995;95:783-96). It was an excellent chronological summary of Dr. Lichtenstein's outstanding research. Many of his publications were instrumental in directing further studies. His contribution to the field of allergy/immunology is much appreciated by members and fellows of the Academy.

I have one concern: Mary Loveless' enormous and seminal contribution on using venom sacs to treat Hymenoptera allergy was not mentioned. It is well known by most allergists and documented in the medical literature that she was the first to use venom for treatment of Hymenoptera allergy. We would like to see her given credit by those who followed and extended her work. Her research preceded that of the Hopkins group by more than 15 years.¹⁻³ Many of us were privileged to know Dr. Loveless and to hear her expound on these studies. Her initial work with Dr. Cook on blocking antibody to ragweed and her work on the efficacy of venom was done in the 1950s through the 1980s. It is surprising that she has not been given an honorary award and recognition by The American Academy of Allergy Asthma and Immunology. Despite the fact that Dr. Loveless is now deceased, this award is long overdue.

Henry B. Freye, MD
41 East Main St.
Mystic, CT 06355

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venom treatment in anaphylactic sensitivity to Hymenoptera sting. *N Engl J Med* 1974;290:1223-7.

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Reply

To the Editor:

I thank Dr. Freye for his kind words about my Presidential address. He is, of course, correct that Dr. Mary Loveless advocated either stinging or using venom sacs to treat Hymenoptera allergy long before we did. In fact, our early work on this subject always referenced her, and my colleague, Dr. Anne Kagey-Sobotka, who did her doctoral thesis research in this area, dedicated it to Dr. Loveless. I should remind Dr. Freye, however, that Dr. Loveless never carried out controlled studies. Further, I question whether her once- or twice-a-year sting regimen was really effective.¹ English beekeepers, who get multiple stings in the summer and fall but who stop beekeeping over the winter, routinely have anaphylaxis during the first few stings the next spring.² Moreover, in developing our treatment regimens, spacing venom injections more than 2 months apart led to a clear increase in treatment failures.³ For these reasons, perhaps, Dr. Loveless failed to convince her fellow allergists, who continued using whole body extracts until we and others demonstrated the clinical efficacy of weekly and then monthly venom injections.

I do regret my oversight but I was, in that address, focusing on our own work, and I have certainly left out the work of others that preceded ours in this and other areas.

Lawrence M. Lichtenstein, MD
Professor of Medicine
Johns Hopkins Asthma and Allergy Center
5501 Hopkins Bayview Circle
Baltimore, MD 21224-6801

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1/8/67055

Gender risk for anaphylactoid reactions to contrast material

To the Editor:

I read with interest the article, "Gender risk for anaphylactoid reaction to radiographic contrast media," by Lang et al. (*J ALLERGY CLIN IMMUNOL* 1995;95:813-7). These authors found the risk of severe contrast media

reactions to be considerably higher in female patients. They point out that although female predominance has been reported in several series of anaphylaxis cases, no definite precedent has been established for greater risk of anaphylactoid reactions caused by radiographic contrast media on the basis of gender. In fact, similar findings have been previously reported.¹ In the only large-scale multi-institutional randomized and blinded study of contrast material reactions published thus far, we originally reported that there were no significant differences in the incidence of reactions occurring in male and female patients.² On later examination of the same data, however, it became clear that if we narrowed the study to a comparison of female and male patients between the ages of 18 and 30 years, the female patients demonstrated a significantly increased incidence of "total reactions," "reactions necessitating therapy," and "grade II reactions."¹

As one potential explanation for the increased incidence in female patients, Lang et al. mentioned the higher dose of contrast media, which might be given to female patients by virtue of their lower average body weights and the use of a fixed contrast material dose. In a large study in which each patient's weight and contrast media dose were recorded, we did find that patients receiving more than 200 mg of iodine per pound of body weight had more than twice the incidence of "reactions requiring therapy" when compared with patients receiving less than 125 mg of iodine per pound of body weight.²

Lang et al. point out that a catamenial exacerbation of asthmatic and anaphylactic potential may exist. In connection with this we have found that the plasmas of both contrast material reactors and asthmatic patients demonstrate an accelerated contact system activity (which would lead to an accelerated bradykinin production) under certain laboratory conditions and that a heparin-like material, believed to be heparan sulfate, appeared to be partly responsible for the priming of these plasmas.³ In vitro studies in the presence of estrogen have shown an increased formation of heparan sulfate in rabbit endometrium as a result of increased sulfotransferase activity and have demonstrated that progesterone suppresses this.⁴ Thus several additional factors may explain the increased incidence of contrast material reactions in female patients.

Elliott C. Lasser, MD
University of California, San Diego
9500 Gilman Dr.
La Jolla, CA 92093

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