

Letter to the Editor

Frequency of mold and pollen mixing in allergen immunotherapy prescriptions within a large health care system, 1990-2010

To the Editor:

Proteolytic enzymes can be found in extracts produced from insects, mites, and molds. Loss of allergen extract potency over time may be attributed to several factors including the activity of proteolytic enzymes.¹ Nelson et al² demonstrated deleterious effects on the potency of pollen extracts when mixed with mold, with the exception of ragweed. Similarly, Grier et al³ also reported a decrease in extract recovery when combining high-protease- and low-protease-containing extracts. The most deleterious effects were seen when cockroach or mold was mixed with trees, grasses, and weeds, again with the exception of ragweed. However, the results of these and other studies are somewhat conflicting.^{4,5}

At the time of publication of the first Allergen Immunotherapy (AIT) Practice Parameter in 1996, data regarding the effects of protease on allergen extracts were lacking.⁶ The 2003 update to the AIT Practice Parameters recommended that molds should not be mixed with pollens, with the exception of ragweed.⁷ Subsequent Practice Parameter updates did acknowledge that conflicting data existed on the stability of ragweed when mixed with mold and recommended that all pollen should be separated from high-protease-containing extracts.^{1,8} We sought to describe the frequency with which mold and pollen are placed in the same AIT prescription in a large health care system and the potential impact of the AIT Practice Parameters on allergen mixing.

The US Army Centralized Allergen Extract Laboratory (USACAEL) formulates AIT extracts for allergy clinics within the Department of Defense, Department of Veteran Affairs, and the Public Health Service. Specific allergen contents of all AIT prescriptions ordered through USACAEL from January 1990 through October 2010 were extracted and analyzed. The total number of AIT prescriptions containing any mold, irrespective of the number of molds, concentration, or manufacturer, was obtained. Prescriptions were then divided into those mixed with and without pollen. Ragweed was excluded from the analysis. The data were then subdivided by patient into single prescriptions (1 injection) and multiple prescriptions (>1 injection). Results were divided into the time period prior to the publication of the first AIT Practice Parameter and each Practice Parameter update (January 1997 to January 2003, February 2003 to September 2007, and October 2007 to October 2010).

USACAEL filled 114,718 AIT prescriptions written for 60,725 patients (Table I). A total of 23.8% (n = 27,307) of all AIT prescriptions contained mold, and of these prescriptions, 46.2% (n = 12,224) also contained pollen. Prior to the publication of the first AIT Practice Parameter (January 1990 to December 1996), 65.2% of mold prescriptions contained pollen. From January 1997 to January 2003, the number of mold prescriptions containing pollen decreased to 49.7%. Following the January 2003 AIT Practice Parameter, wherein a specific recommendation on separation of molds and pollen (except ragweed) was published, the number of mold prescriptions containing pollen fell to 32.2% (February 2003 to September 2007 = 33.8%, October 2007 to October 2010 = 29.8%) (Table II).

TABLE I. USACAEL prescriptions: 1990 to 2010

Time period	n
January 1990 to December 1996	13,300
January 1997 to January 2003	49,204
February 2003 to September 2007	31,566
October 2007 to October 2010	20,648

While there is an overall reduction in AIT prescriptions that contain a combination of mold and pollen, this trend differs significantly when comparing single-injection (SI) and multiple-injection (MI) prescriptions. Prior to the publication of the first AIT Practice Parameter (January 1990 to December 1996), 81.8% of SI mold prescriptions contained pollen, compared with only 51.9% of MI prescriptions. From January 1997 to January 2003, the number of SI mold prescriptions mixed with pollen decreased to 75.0% and only 30.7% of MI mold prescriptions contained pollen. The period spanning the January 2003 AIT Practice Parameter through the next update published in September 2007 coincided with a further decrease in mixing of mold and pollen in SI and MI prescriptions to 68.4% and 20.3%, respectively. Although MI prescriptions containing mold mixed with pollen continued to decrease to 16.2% from October 2007 to October 2010, SI prescriptions demonstrated an increase to 72.3% (Tables III and IV).

During the overall time period studied, 46.2% of AIT prescriptions with mold also contained pollen. Of the 3,334 mold AIT prescriptions written between January 1990 and December 1996, pollens and molds were mixed 65.2% of the time. The first AIT Practice Parameter published in January 1997 initially raised concerns for the effects of proteases, but it did not offer specific mixing recommendations.⁶ From the time of this publication until the next AIT Practice Parameter was published in January 2003, mixing of molds and pollens was reduced to 49.7% of 13,205 prescriptions. These percentages continued to decrease with each subsequent Practice Parameter update, suggesting that specific mixing recommendations set forth in the AIT Practice Parameters led to a change in prescribing patterns among providers. Yet, from the period spanning October 2007 to October 2010, 29.8% of total mold prescriptions still continued to contain pollen. Esch⁹ previously examined 582 AIT prescriptions ordered by 20 different allergists in the United States and found that nearly one third of prescriptions contained combinations of protease-containing allergen extracts (fungal or insect) and pollen allergen extracts. Cost and patient compliance were cited by prescribers as the most common reason for combining allergen groups. In our study, cost should not be a factor as USACAEL does not place the financial burden for AIT on individual patients, providers, or clinics. Patient compliance may be a driving factor, as one injection can be perceived as less painful and more convenient. Esch found that glycerinated extracts were requested for only about half of these prescriptions, whereas all USACAEL extracts are glycerinated, though the glycerin content of each individual extract formulation is variable. This may also factor into the observed prescribing patterns, as studies have demonstrated that the presence of glycerin in allergen extracts may preserve potency.³ To date,

TABLE II. Mold allergen immunotherapy: all prescriptions

January 1990 to December 1996 (n = 3,334)		January 1997 to January 2003 (n = 13,205)		February 2003 to September 2007 (n = 6,818)		October 2007 to October 2010 (n = 3,950)	
Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen
1,160	2,174	6,637	6,568	4,512	2,306	2,774	1,176
34.8%	65.2%	50.3%	49.7%	66.2%	33.8%	70.2%	29.8%

TABLE III. Mold allergen immunotherapy: SI prescriptions

January 1990 to December 1996 (n = 1475)		January 1997 to January 2003 (n = 6018)		February 2003 to September 2007 (n = 1914)		October 2007 to October 2010 (n = 953)	
Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen
267	1208	1503	4515	604	1310	264	689
18.2%	81.8%	25.0%	75.0%	31.6%	68.4%	27.7%	72.3%

TABLE IV. Mold allergen immunotherapy: MI prescriptions

January 1990 to December 1996 (n = 1859)		January 1997 to January 2003 (n = 6679)		February 2003 to September 2007 (n = 4904)		October 2007 to October 2010 (n = 2997)	
Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen	Mold only	Mold and pollen
893	966	4626	2053	3908	996	2510	487
48.1%	51.9%	69.3%	30.7%	79.7%	20.3%	83.8%	16.2%

no study has looked at the clinical impact of AIT when mixing mold with pollen.

In conclusion, we have observed a significant reduction in AIT prescriptions that contain molds mixed with pollen. There seems to be a strong temporal relationship between the publication of specific mixing recommendations in the AIT Practice Parameters and these observed changes in prescribing patterns. Despite these recommendations, a significant number of prescriptions continue to mix mold with pollen, particularly among SI prescriptions. The reasons behind such prescribing patterns and its clinical impact deserve further study.

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