

Letter to the editor

Optimal maintenance dose immunotherapy based on major allergen content or potency labeling

The recent review article in *Allergy*, “Efficacy of specific immunotherapy in allergic asthma: myth or reality?” by Bonifazi & Bilò, discusses the possible clinical advantages of determination of the microgram content of major allergens in extracts used for immunotherapy (1). The authors state that such a determination will allow the physician to aim at an optimal maintenance dose of 6–12 µg of the major protein when treating pollen allergy. This is in close concordance with the recent position statement of the American Academy of Allergy, Asthma, and Immunology (AAAAI) on the use of standardized allergen extracts (2). The AAAAI statement notes that achieving a maintenance dose of approximately 5–20 µg of major allergen per injection is associated with significant improvement in patient symptom scores. However, Bonifazi & Bilò take this one step further and compare these microgram values with the arbitrary values of the US Food and Drug Administration (FDA) allergy unit (AU), as reported in a ragweed study by Creticos et al., in which the Amb a 1 allergen content was measured in micrograms (3). According to the FDA requirements, this ragweed extract was at that time labeled in allergy units based on RAST-inhibition results compared to an established ragweed reference extract. (Incidentally, this extract is no longer labeled in AU but only in Amb a 1 content.) Later in the study, the major allergen content in a *D. pteronyssinus* study by Haugaard et al., using a 100 000 SQ ALK (Denmark) extract (4), is correlated to the FDA AU unit.

However, in the first example, it is not correct to assume that microgram dosages are the same in all standardized extracts only when specifically measured. As found with US standardized cat hair extract years ago, the potency labeling may not correlate to the biologic activity determined by skin testing. This finding mandated a change from labeling the extracts in AU to BAU and an adjustment of the reference range based on Fel d 1. Thus, the FDA references or reference materials may change and so may the microgram content, although the potency labeling is the same. In the

latter example of Haugaard et al.’s dust-mite study, it is incorrect to state an AU value because neither the skin-test potency based on the FDA procedure nor the ELISA-inhibition results were established in this extract used by Haugaard et al. (4). It is important to recognize that the major allergen content may differ sixfold even though the potency labeling is the same, as Chapman et al. reported some years ago (5). In relation to the mite extracts, it is known that the amount and ratio of mite group I and II allergens in US and European extracts may differ due to the different source material and extraction procedures for mites (6).

Apparently, it is important to reiterate that the strength of an extract measured in arbitrary units such as BU or FDA BAU cannot be compared. They are defined by two very different skin-test protocols (skin prick test and intradermal skin test) in two differently selected patient populations. The biologic unit will reflect only the strength of the skin-test response obtained according to a defined skin-test procedure with a particular extract. The FDA AU describes only a relative value correlated to the ELISA/RAST-inhibition results obtained from an established reference extract and does not include a biologic estimation of skin-test potency.

We must keep in mind the following points:

- A biologically standardized extract gives the physician useful information about the cutaneous response that can be expected when the extract is used for specific diagnosis. In the case of treatment, the skin is not necessarily a relevant parameter for determining biologic efficacy.
- The same standardized allergen may show different major allergen content even though the potency measured by skin testing is the same.

It has been recommended that the content of major allergens in some biologically standardized extracts be evaluated so that safety and efficacy may be related to the microgram content of the major allergen administered. This seems to be an effective approach to optimize the treatment results.

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However, I view with caution the assumption that, because an extract is potency-labeled according to a given standardized method, it will also reflect the major allergen content. Currently, there is no requirement for manufacturers to adjust or label their extracts according to major allergen content (excluding ragweed and cat hair). Potency is based on certain general potency criteria which constitute the sum of several factors, among which major allergen content is an important one. It would be advantageous if the amount of major allergen content is known in the extracts used for immunotherapy so that in the future we can compare immunotherapy schedules and dosages in order to assess the risk of side-effects and the efficacy, as Bonifazi & Bilò suggest in their very excellent review article on immunotherapy (1).

References

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