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Impact of biologic variation on latex allergenicity

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I read with interest the position statement on the use of standardized allergen extracts (J Allergy Clin Immunol 1997;99:583-6) and recall the article by Hamilton et al. (J Allergy Clin Immunol 1996;98:872-83) on the development of a characterized latex skin-testing reagent. The position statement emphasized the importance of a *consistent relationship* between the allergen being measured and other allergens present in the extract. Establishing a reference reagent prepared from whole *Hevea* latex, rather than purified proteins, is no simple task. Latex allergy stems not from a single allergen but from no less than seven latex proteins (Hev b 1 to Hev b 7). These proteins could differ in their relative allergenicity; they certainly vary widely in their relative abundance in natural rubber latex. Hevein (Hev b 6), for example, is the most abundant soluble protein in latex, constituting some 22% of the total soluble latex proteins. This figure is even higher if we include its precursor, prohevein, which is another major latex protein carrying the hevein allergenic epitopes. Thus one allergen in a latex preparation can be of a concentration tens or hundreds of times greater than that of another. A patient who is only marginally allergic to hevein might very well have a strongly positive test response to a whole-latex reference preparation simply because there is so much hevein present. On the other hand, a patient who is allergic to another allergen that is underrepresented in latex might have a negative test response.

My associates and I have found statistically significant seasonal differences (up to 25-fold) in the allergenicity of latex from three of the most widely planted *Hevea* clones. The total level of soluble allergens, as determined by competitive inhibition assays, does not reveal whether the individual latex allergens all follow the same trend in seasonal variation; further complications ensue if they do not. Clearly, it would take more than simple dilution or concentration to adjust a reference reagent prepared from whole latex to match a predetermined level of allergenicity.

The reproducibility of Hamilton's latex allergen reagent would likely be adequate if the allergens used were in molar excess (nonlimiting) to the IgE antibody in the skin or blood. Such a reagent would generate a positive or negative test result but would not be

quantitative. On the other hand, the use of a whole-latex reference reagent to assay for residual allergens present in a latex product (e.g., by an inhibition assay) needs to be considered critically. Such an assay would need to be quantitative and would introduce yet another variable (i.e., the allergen composition of the article being tested).

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PII: S0091-6749(98)70215-5

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