

Guanine – an adequate index of mite exposure?

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Of the three methods of assessing exposure to house-dust mite allergens, mite counts, allergen immunoassays, and the guanine assay, only the guanine test can be performed in a doctor's office. This makes the test convenient for allergists, other practitioners, and patients themselves, allowing a measure of mite allergen exposure in the home, without recourse to sophisticated laboratory techniques. But does the guanine test accurately reflect mite allergen exposure? This question is addressed by two papers in the current issue. Quoix et al. argue that the guanine test is a simple, inexpensive, and predictive method for assessing mite allergen levels (8). In contrast, Hallas et al. have evidence that the test measures guanine from sources other than house dust and is therefore of limited clinical value (3).

Guanine is the major nitrogenous waste product of arachnids, and the use of the test is based on the fact that mites are the most common source of guanine in house dust, spiders notwithstanding. Tests for guanine were first applied to house-dust analysis by Bischoff & Schirmacher and van Bronswijk et al. (1, 2). Dust samples are incubated in alkaline alcohol solvent to extract the guanine, which is then detected colorimetrically by its interaction with diazonium compounds and the formation of guanine azo-dye. A semiquantitative dipstick test (marketed as the Acarex test) grades the color/guanine content on a four-point scale: class 0, yellow, <0.06% guanine; class 1, light red, 0.06-0.25%; class 2, red, 0.25-1%; class 3, dark red, >1% guanine (4, 6, 10). The color reaction can also be read in a spectrophotometer and compared to a standard curve for a quantitative assay, measuring guanine in µg/ml.

Previous studies have shown that guanine assays "correlate" with several other methods of measuring mite allergens, including skin tests, RAST inhibition,

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crossed immunoelectrophoresis, and, most recently, ELISA for *Der p 1* and *Der f 1* (4-6, 9, 10). The correlations with Group I allergen levels are of most interest because of the recommendations that specific levels of Group I allergen exposure should be regarded as risk factors for sensitization (2 µg/g dust) or for exacerbations of asthma attacks (10 µg/g dust) (7). Four studies have compared Group I allergen levels with the semiquantitative guanine test, in over 500 dust samples in all (4, 5, 9, 10). Mean data with ranges are shown in Table 1. The consensus from these studies is that samples with guanine class 0 are likely to contain <2 µg/g Group I allergen, whereas samples with class 2 or 3 contain >2 µg/g in all cases, and in most cases (~80%) contain >10 µg/g. The studies consistently show widest variation in allergen levels for guanine class 1; consequently, those values are most difficult to interpret.

In a follow-up study of 239 dust samples they had studied previously, Quoix et al. compared the sensitivity and specificity of the semiquantitative guanine test in relation to Group I allergen levels. In addition, they used receiver operating characteristic (ROC) curves to compare true positive and false positive rates at different guanine concentrations (8). The results for the semiquantitative guanine assay were similar to those reported previously. The negative predictive value of guanine class 0 was 87%, and the positive predictive values of classes 2 and 3 for samples containing >10 µg/g allergen were 88% and 100%, respectively. The ROC curves showed that all samples containing <900 µg guanine contained <2 µg/g allergen and that a guanine content of >3000 µg/g was the best indicator of samples containing >10 µg/g allergen (sensitivity 88%, false positives 7%). So far, so good for guanine. However, Quoix et al. acknowledge that class 1 guanine

Table 1. Guanine and *Dermatophagoides* Group I allergen levels – data from three studies*

Study	Guanine class			
	0	1	2	3
van der Brempt et al. (10) (n=177)	0.5 (0.1–9)	4.4 (0.1–117)	16.4 (2–260)	31.8 (6–156)
Hoyet et al. (4) (n=239)	1.7 (0.1–12)	5.7 (<0.1–26)	35.2 (4–102)	131.3 (24–481)
Ransom et al. (9) (n=37)				
> 10 µg/g	0	1	5	5
2–10 µg/g	0	10	2	0
< 2 µg/g	8	6	0	0

* Table shows mean Group I allergen levels for each guanine class, with ranges shown in parentheses. For the study by Ransom et al., the numbers of positive samples at different Group I concentrations are shown.

remains a problem and suggest that for these dusts a second sample be obtained and assayed by quantitative guanine assay.

Hallas et al. question the test on two grounds. First, they found that the assay measures xanthine in addition to guanine; second, they found that all dust samples (51 in all) contained more guanine than could be “explained” by their Group I content (3). These studies were prompted by the authors’ accidental observation that wheat flour showed a moderate reaction in the Acarex test in the apparent absence of mites. Xanthine accounted for 2–15% of the “guanine” in *Dermatophagoides pteronyssinus* or *D. microceras* cultures, but was not detected in *D. farinae*. Thus, the influence of xanthine appears to be relatively small. To estimate the relationship between Group I allergen levels and guanine content, the authors assayed eight mite cultures for both products and used the Group I levels as a conversion factor to predict guanine levels in the dust extracts. They then assayed the dusts by quantitative guanine assay and compared guanine “explained” by Group I with that found in the samples. The formula is rather obscure, in part because the data showing mite-derived Group I and guanine levels are not presented, and it is not clear what conversion factors were used. The authors found that all the dust samples appeared to contain more guanine than could be explained on the basis of the Group I values, particularly samples containing < 10 µg/g allergen, where only 17% of the guanine appeared to be related to allergen production. However, for samples containing > 10 µg/g allergen, a much better correlation was obtained, and a mean of 40% guanine could be explained on the basis of allergen levels.

Hallas et al. suggest that much of the guanine in house dust is derived from exogenous sources, but mention only two possibilities: plants, which are

more likely to contain xanthine, and storage mites. These suggestions seem rather weak, particularly since storage mites are well known to cause allergic reactions, even though they do not produce allergens homologous to the *Dermatophagoides* Group I. While it is true that the presence of guanine cannot be unambiguously ascribed to dust mites, it is also clear that there is a strong probability that dusts containing > 3000 µg/g guanine contain > 10 µg/g Group I allergen. In fact, comparisons of this figure, suggested by the study of Quoix et al., with the data of Hallas et al. fit very well. On the basis of current evidence, the guanine test appears to be a useful screen for mite allergen exposure. Classes 0, 2, and 3 provide a good indication of either the presence or absence of mite allergens, with class 1 remaining a gray area; that is, a qualified “yes” in answer to the question posed at the beginning of this paper.

The attraction of a dipstick test, such as the guanine assay, is that it provides a simple and inexpensive method of assessing indoor allergen exposure for both doctor and patient alike. It is hoped that the further development of such tests, including monoclonal-antibody-based detection tests, will make it easier for allergists to investigate the home environment and encourage patient compliance with allergen-avoidance procedures.

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