

Letter to the Editor

Comparison between AlaTOP and IP8 inhalant panels on the Immulite 2000 analyzer

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Atopic allergy analysis is based on clinical presentation, family history, skin prick tests and specific IgE antibodies in serum. The advantage of measuring specific IgE (sIgE) is that it is non-invasive and that many tests can be performed using a single serum sample. To prevent unnecessary laboratory testing, it is common to use a screening test containing the most prevalent allergens. For this purpose we use the AlaTOP® panel in our laboratory. Recently, several alternative inhalant panels were developed by DPC, of which the IP8 panel more closely represents the most common allergens in the Dutch population. In the present study we evaluated the diagnostic performance of the AlaTOP and IP8 panels compared with sIgE. AlaTOP, IP8 and sIgE are routinely measured on the third-generation Immulite 2000 Allergy system (Diagnostic Product Corporation DPC, Los Angeles, CA, USA). The performance of the Immulite 2000 immunoanalyzer and clinical evaluation of AlaTOP have previously been described by Cobbaert et al. in detail (1).

The AlaTOP results compared well with clinical symptoms, patient history and in vivo skin tests, with a relative sensitivity of 91% for their study diagnosis. Furthermore, Yilmaz et al. (2) found a sensitivity of 83% in atopic adults with atopic dermatitis, asthma or hay fever, the presence of at least one positive sIgE and family history. The AlaTOP test has been designed for the worldwide market using an aero-allergy panel from 12 sources with maximal cross-reactivity. Despite its high sensitivity, both groups suggested a modification of the AlaTOP composition based on the presence of locally important allergens (1, 2). Some of the allergens included are rare in The Netherlands, such as Bermuda grass, Japanese cedar, *Alternaria tenuis* and common ragweed (*Ambrosia*) and show little cross-reactivity with European allergens. We therefore reasoned that its sensitivity could

be further improved by replacing the above-mentioned allergens with more prevalent allergens, such as mugwort (*Artemisia vulgaris*, w6). Inhalant panel IP8 fulfils these criteria. In addition, mugwort pollen is abundant in northwestern and central parts of Europe. Recently, mugwort allergy has attracted much attention because of its cross-reactivity with the Asteraceae family and has been identified as the cause of occupational disease among greenhouse workers in the Dutch flower industry (3–5). Furthermore, clinically relevant cross-reactivity has been described between mugwort and chamomile infusions (6), celery and carrot, referred to as celery-carrot-birch-mugwort-spice syndrome (7). Although ragweed allergy is not yet significant in The Netherlands, in contrast to Southern Europe, an increase in ragweed pollen was measured in October 2006. Furthermore, since the major allergens for ragweed (Amb a 1) and mugwort (Art v 1) are unrelated proteins (8), this might warrant a screening test containing both ragweed and mugwort.

The IP8 panel consists of house dust mite (*Dermatophagoides pteronyssinus*, d1), cat dander epithelium (e1), dog dander (e5), timothy grass (g6), cultivated rye grass (g12), *Cladosporium herbarum* (m2), birch (t3) and mugwort (*Artemisia vulgaris*, w6). The composition of the AlaTOP test is as follows: house dust mite (*Dermatophagoides pteronyssinus*, d1), cat dander epithelium (e1), dog dander (e5), Bermuda grass (g2), timothy grass (g6), *Penicillium notatum* (m1), *Alternaria tenuis* (m6), birch (t3), Japanese cedar (t17), common ragweed (*Ambrosia artemisiifolia*, w1), English plantain (w9), and *Parietaria officinalis* (w19).

In this study, we therefore compared AlaTOP and IP8 for 183 serum samples. In the case of a positive result for one or both of the inhalant panels, a set of six sIgEs was also measured: d1, e1, e5, g6, t3, w6. For negative results, three additional panels were measured: gp3 (sweet vernal grass, perennial rye grass, timothy grass, cultivated rye grass, velvet grass), tp9 (alder, birch, hazelnut, oak, willow), and mp1 (*Penicillium notatum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Candida albicans*, *Alternaria tenuis*). The combination of a negative screening test and a positive result for one of the sIgEs or sIgE panels was designated as a false negative (FN). By analogy, the combination of a positive screening test and negative results for all sIgEs and sIgE panels was designated as a false positive (FP). When there was no discrepancy between the screening test and sIgEs, with both negative or both positive, this was designated as a true negative (TN) or true positive (TP), respectively. Total agreement (TA) was calculated as

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Table 1 Distribution between IP8 and AlaTOP for 183 serum samples.

IP8	AlaTOP						
	Class 0	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Class 6				3	1		
Class 5					3	1	1
Class 4			1	7	2	5	
Class 3	2 ^e	3	8	3	2		
Class 2	8 ^d	10	5	3			
Class 1	1 ^c	5	4				
Class 0	80	24 ^a	1 ^b				

^aFN (IP8), 15×d1, 1×e1, 1×g6; FP (AlaTOP), 7×; ^bFN (IP8), 1×d1; ^cFN (AlaTOP), 1×g6; ^dFN (AlaTOP), 8×g6; ^eFN (AlaTOP), 1×w6; FP (IP8), 1×.

Table 2 Performance of inhalant panels AlaTOP® and IP8 relative to specific IgE.

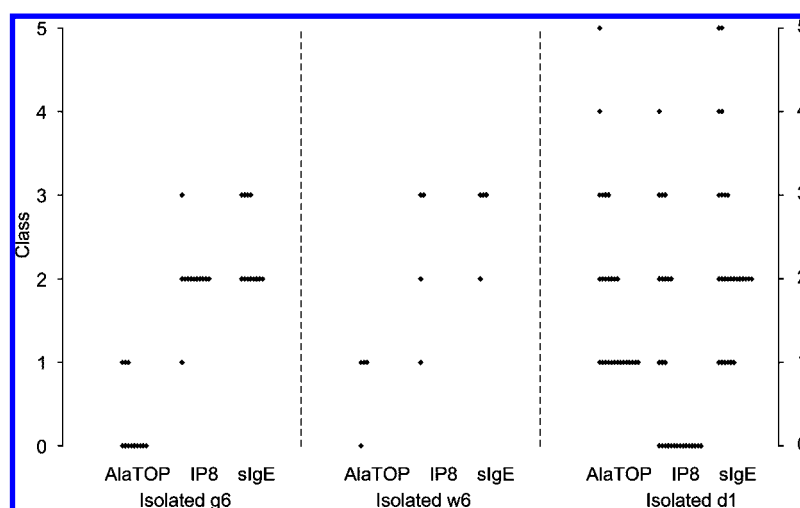
	AlaTOP®	IP8
True positives, n	85	77
True negatives, n	81	87
False positives, n	7	1
False negatives, n	10	18
Total agreement, %	91	90
Relative sensitivity, %	89	81

(number of results – number of discrepancies) × 100% / number of results. To include all allergens occurring throughout the year, samples were collected during a 12-month period. To obtain a sufficient number of samples around the cutoff value, approximately 50/183 samples with AlaTOP values between 0.7 and 1.3 were randomly selected. The cutoff value for IP8 and slgE is 0.35 kU/L and for AlaTOP is set at 1.0, which is calculated as 2.5 × sample count relative to the count for the lowest adjustor. For comparability, the AlaTOP and IP8 results are recalculated into the following classes (0–6): AlaTOP, <1, 1–2, 2–10, 10–50, 50–143, 143–286, and >286; IP8, <0.35, 0.35–0.70, 0.70–3.5, 3.5–17.5, 17.5–50, 50–100, and >100 kU/L.

The analytical performance of the AlaTOP and IP8 screening tests is shown in Tables 1 and 2. The relative sensitivity for both AlaTOP and IP8 (Table 2) is

lower than might be expected considering that the AlaTOP, IP8 and slgE are all from the same company. The relative insensitivity of the AlaTOP test can largely be ascribed to the high number of FN results for isolated timothy grass pollen (g6) (9/10), whereas the IP8 relative insensitivity is due to the high number of FN results for isolated house dust mite (d1) (16/18) (Table 1, Figure 1). Furthermore, using AlaTOP only 3/12 samples with positive slgE for isolated g6 were correctly identified (range 1.10–1.50, class 1) and 12/27 samples with positive slgE for isolated d1 were correctly identified with IP8 (range 0.41–27.0, class 1–4) (Figure 1). In contrast to our findings, Cobbaert et al. (1) were not able to demonstrate a discrepancy between AlaTOP and PhadiaTOP test based on a single slgE. This may have been caused by variation between lots, as re-analysis of samples from three patients with isolated g6 slgE resulted TP results in all cases using a different lot number. Furthermore, AlaTOP screening resulted in one FN result for isolated mugwort (w6) slgE and marginally positive AlaTOP results (range 1.04–1.08, class 1) for another three samples. The class 1 result was probably due to cross-reactivity with ragweed (w1) present in AlaTOP. IP8 correctly identified 4/4 isolated w6 slgE (Figure 1).

It is important to note that all FN results for both AlaTOP (g6, w6) and IP8 (d1, e1, g6) were observed in isolated positive slgEs (n=28) and that all com-

**Figure 1** AlaTOP and IP8 results for serum samples from patients with isolated timothy (g6) slgE (n=12), isolated mugwort (w6) slgE (n=4) and isolated house dust mite (d1) slgE (n=27).

bined positive sIgEs were correctly identified by both AlaTOP and IP8 ($n=67$). This is probably caused by a relative deficit of the allergen concerned in the allergen mixture and/or a lack of samples with isolated sIgEs in the calibration procedure. The number of FP results for AlaTOP ($7/183=3.8\%$) and IP8 ($1/183=0.5\%$) is of minor clinical importance.

In conclusion, a quality control survey with isolated sIgEs is required for timely identification of batch problems with an inhalant screen test (AlaTOP or IP8). The AlaTOP sensitivity for timothy grass pollen should be improved. If the sensitivity of IP8 for house dust mite is improved, this inhalant screen test is an interesting alternative for AlaTOP in Europe. The necessity to add ragweed to the IP8 panel should be further investigated.

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