

Original article

A comparison of different allergometric tests, skin prick test, Pharmacia UniCAP[®] and ADVIA Centaur[®], for diagnosis of allergic diseases in children

Background: The diagnosis of allergic disease is performed by skin prick tests (SPT) or through the demonstration of specific IgE in a blood sample via an *in vitro* test. The measurement of IgE concentration against allergens provides critical information in clinical allergy. Standardized and reproducible methods contribute to the quality of diagnosis and treatment of allergic disease.

Methods: In this study we evaluated the performance of a new specific IgE method, developed by ALK-Abellø for Bayer Diagnostics to run on their ADVIA Centaur immunoassay system. One hundred and fifty-one children with allergic diseases (both food and inhalant allergies) were tested for specific IgE (sIgE) via SPT and *in vitro* tests (UniCAP system, Pharmacia, and ADVIA Centaur immunoassay system, Bayer Diagnostics) and the test results were correlated with the clinical data.

Results: Statistical analysis revealed no significant difference between the two *in vitro* tests compared with clinical history. The sensitivities and specificities are similar, but the UniCAP system method has higher sensitivity. In the children with cow's milk allergy, the UniCAP system has sensitivity of 91% and specificity of 70%; the ADVIA Centaur immunoassay has sensitivity of 82% and specificity of 74%. In hen's egg allergy, UniCAP system has 94% sensitivity and 64% specificity, and the ADVIA Centaur system has 88% sensitivity and 52% specificity. In inhalant allergies, the two methods show statistically similar performances for both grass pollen allergies (UniCAP sensitivity 100%, specificity 73%; ADVIA Centaur sensitivity 95%, specificity 79%) and in the dust mites allergies (UniCAP sensitivity 91%, specificity 62%; ADVIA Centaur sensitivity 86%, specificity 64%). In cat allergies, the systems showed equivalent results (UniCAP sensitivity 100%, specificity 71%; ADVIA Centaur sensitivity 100%, specificity 70%). Using the UniCAP system, the geometric mean of sIgE values in children with clinical allergy is significantly higher than in sensitized ones. The ADVIA Centaur system shows a similar trend with the exclusion of cow's milk and *Dermatophagoides farinae* allergens. With this last method the mean value of sIgE is higher in sensitized than in symptomatic children.

Conclusion: The new ADVIA Centaur method compares favorably with the results obtained on the UniCAP system. If other studies continue to confirm this data, then the advantages are numerous: the use of only a small quantity of serum (25 µl per allergen), rapid turnaround time, minimal hands-on time, and no interference from IgG.

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The basis for an etiologic diagnosis of allergic disease is the demonstration of a sensitization, namely the presence of specific IgE antibodies. While a clinical history may be sufficient to identify causes and judge the severity of some allergic diseases, sometimes the history is complex and many allergens may be involved. To identify the etiologic allergen, we may apply clinical tests such as direct challenges or avoidance trials. These tests are complex

and usually performed for food allergies. To diagnose inhalant allergies, allergometric assessment—if associated with an accurate history—is the routine and simplest available method (1). To identify the causative allergen, the assessment can be performed *in vivo* by skin prick tests (SPT) or *in vitro* by measuring allergen-specific IgE. Reliable and accurate assessment of specific IgE is essential to reach a correct diagnosis (2, 3). There are

several automated and semiautomated *in vitro* methods to identify specific IgE, all with varying menus, technologies, and performance, including: CAP System FEIA by Pharmacia & Upjohn Diagnostic (Uppsala, Sweden); MAGIC LITE manufactured by ALK-Abelló for Bayer Diagnostics (Tarrytown, NY); AlaSTAT and Immulite by Diagnostic Products Corporation (Los Angeles, CA); HY-TEC by Hycor Biomedical, Inc. (Garden Grove, CA); Access by Beckman Coulter, Inc. (Fullerton, CA).

We evaluated the performance of a new specific IgE method for the ADVIA Centaur, which is manufactured by ALK-Abelló for Bayer Diagnostics. We are reporting the results of a study involving 151 children with allergic diseases, comparing ADVIA Centaur results with the UniCAP system results and SPT results, in relation to clinical diagnosis.

Material and methods

Study population

The study enrolled 151 consecutive referrals to the Allergologic Center of the Pediatric Department of Bologna University, between January and July 2000. The children ranged in age from 4 months to 14 years (median 70 months), and the majority were boys (boys/girls = 89/62). All the children presented allergic diseases: 62 with atopic eczema/dermatitis syndrome (AEDS) (4) defined by the criteria of Hanifin and Rajka (5); 39 with asthma; 36 with rhinitis; and 14 with allergic urticaria/oral allergy syndrome (U/OAS). Some children also presented other allergic symptoms of less clinical relevance. In the group of children with atopic dermatitis, 12 presented with U/OAS; of the 36 children with rhinitis, 23 also had mild symptoms of AEDS, and 4 others demonstrated symptoms of U/OAS. Moreover, 17 of 39 children with asthma showed mild allergic rhinitis, and 8 others showed symptoms of AEDS.

The diagnosis of allergic disease, specifically inhalant allergy, was made when all three of the following factors were present: a) the clinical history provided accurate orientation to a specific inhalant allergen; b) the allergic disease appeared or worsened when allergen exposure occurred; c) one of the *in vivo* or *in vitro* tests confirmed the previous orientations.

Diagnosis of food allergy was performed via provocation food challenge, by giving the children successive doses of the suspected allergen, either freshly pasteurized cow's milk (CM) or mixed hen's egg (HE). Successive doses of raw HE (egg-white and yolk) were 0.1, 0.3, 1, 3, 10, and 20 ml. Similar successive doses of fresh pasteurized milk were made up to 100 ml. The time interval between each dose was 15–30 min. The test was stopped if clinical symptoms were observed or when the highest dose was reached. Children were observed in the hospital for the first 6 h after the challenge, and then for 7 days at home. The food challenges were scored by a pediatric allergologist and considered positive if a single symptom, or a combination of the following reactions, was observed: allergic urticaria, angioedema, wheezing, vomiting, diarrhea, abdominal pain, shock, or exacerbation of AEDS.

Skin prick tests

Skin prick tests were performed following established guidelines. The patients took no antihistamines of any type for at least 7 days before the prick tests. Allergen extracts (Laboratorio Lofarma,

Milan, Italy), along with appropriate negative (saline) and positive (histamine) controls, were applied on the forearm using the prick technique. The following allergens were tested: CM, HE, grass pollen, cat, *Dermatophagoides pteronyssinus*, and *D. farinae*. Other allergens were tested on the basis of the child's history, but are not included in the results of this study. Allergens eliciting a mean wheal diameter of 3 mm or greater than the negative control were considered positive. No side effects were observed during the skin prick tests. In a small number of patients, the tests could not be performed because there had been difficulty stopping previous antihistamine therapy.

Serum samples

Serum obtained during each child's initial visit was divided into two 1.5–2 ml aliquots, given an identification number, then stored at –20°C. The sera were then simultaneously analyzed blindly on the ADVIA Centaur immunoassay and the UniCAP system.

Allergens/assay procedures

Tests for specific IgE were assessed in all patients for the following seven allergens: *D. pteronyssinus* (d 1), *D. farinae* (d 2), cat dander (e 1), Bermuda grass (*Cynodon dactylon*, g 2), timothy grass (*Phleum pratense*, g 6), CM (f 1), HE (f 2); each assayed on both the UniCAP and ADVIA Centaur systems.

The CAP System FEIA employs a type of “architecture” whereby the allergen of interest is covalently bound to a hydrophilic carrier polymer, encased in a capsule, which catches all allergen-specific IgE in the sample. Allergen-specific IgE is detected directly with a combination of polyclonal and monoclonal anti-IgE (F_c) antibodies labeled with beta-galactosidase, generating fluorescence.

The ADVIA Centaur specific IgE assay is a reverse sandwich immunoassay (Fig. 1) using direct chemiluminescent technology. The monoclonal mouse antihuman IgE antibody is covalently bound to paramagnetic particles (PMP) in a solid phase. The anti-IgE coupled to the PMP captures the sample IgE. Non-IgE is removed by washing. Biotinylated allergen is added in excess and binds to the allergen-specific IgE antibody captured on the solid phase. Acridinium ester-labeled streptavidin in the LITE reagent binds to the biotin-labeled allergen. A direct relationship exists between the amount of allergen-specific IgE present in the sample and the amount of relative light units detected by the system.

The detection limit of the CAP System FEIA and ADVIA Centaur system is 0.35 kU/l sIgE. Children were considered sensitized if their specific IgE levels were above the detection limit. In case of pollinosis, when comparing an *in vitro* specific IgE test with a clinical evaluation, we considered it sufficient to define a positive *in vitro* test if only one of the two allergens studied (Bermuda grass g 2, or Timothy grass g 6) gave a positive result. Similarly we analyzed *D. pteronyssinus* and *D. farinae* to diagnose perennial respiratory allergy.

Statistics

We considered as the reference the clinical diagnosis of allergic disease. Differences in sensitivity and specificity between the ADVIA Centaur and UniCAP sIgE assays for the same allergens were determined and evaluated to see if they were statistically significant. (In this study, significance will imply two-sided tests and confidence intervals at 95% confidence.) Each sample was assayed by both methods.

Because of the pairing, we were able to correlate the sensitivity and specificity of the first method with those of the second. For

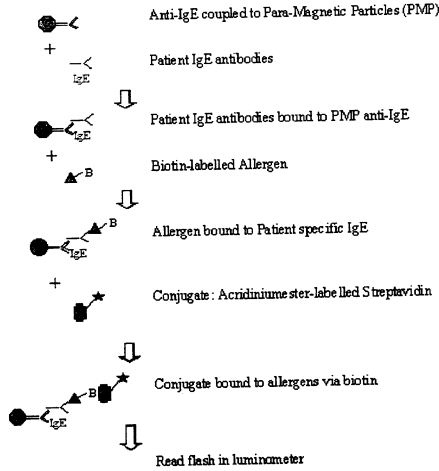


Figure 1. Architecture of the ADVIA Centaur sIgE assay.

example, consider a set of patient samples with positive reference values (e.g. patients whose history indicates that they are allergic to the allergen under consideration): the numbers of samples, positive or negative, in each of the assays can be put into a 2×2 array (Fig. 2). The formula for determining the total number of samples with results for both assays and with positive reference values is:

$$n = a + b + c + d$$

The sensitivity for Assay 1 (S_1) is the probability that Assay 1 will be positive given that the reference value is positive. This is estimated using the formula:

$$S_1 = (a + b)/n$$

Similarly,

$$S_2 = (a + c)/n$$

is the probability that Assay 2 will be negative given that the reference value is negative. The difference in sensitivities is:

$$\delta = S_1 - S_2 = [(a + b)/n] - [(a + c)/n] = (b - c)/n$$

The difference in sensitivities is defined so that it is positive if Assay 1 is more sensitive than Assay 2 and negative if Assay 1 is less sensitive than Assay 2.

To judge if the difference was significantly different from zero, we tested against a null hypothesis that the difference was zero. In which case, b and c should be identical, so we replaced each by their mean. Then $b - c$ becomes zero and the expression for the standard error becomes:

$$SE(\delta) = (1/n)\sqrt{(b + c)} \text{ under } H_0 : \delta = 0$$

The hypothesis was tested using the normal statistic

$$Z = \delta/SE(\delta)$$

after a continuity correction to the numerator. This gives:

$$z = \{|\delta| - (1/n)\}/SE(\delta) = (b - c - 1) / \sqrt{(b + c)}$$

z is compared to the critical normal value for a two-sided test at the desired confidence level (1.96). The square of the z statistic may be compared to a χ^2 distribution with one degree of freedom:

$$\chi^2 = (|b - c| - 1)^2 / (b + c)$$

Assay 1	Positive	a	b
	Negative	c	d
		Positive	Negative

Assay 2

Figure 2. 2×2 array for assay positive and negative samples.

The critical χ^2 value (3.84) is the square of that for z ($3.84 = 1.96^2$). As a χ^2 test, this is referred to as McNemar's test. However, because the standard error used in McNemar's test differs from that used in calculating the confidence limits (i.e. replacing both b and c by their mean), and because the hypothesis test includes the continuity correction, the confidence interval may exclude zero (i.e. both ends are positive or both are negative) when the hypothesis test indicates that the difference is not significant.

Our specificity calculations are essentially the same as those for sensitivity differences, except that we used only those samples that had negative reference values.

Results

Clinical outcomes

The diagnosis of HE allergy was evaluated in 40 cases, and CM allergy in 27 cases. In children with HE allergy, SPT were available only in 34 patients and were found positive in 31/34 cases (91.2%), tests using the sIgE CAP system were positive in 38/40 (95%), and using the sIgE ADVIA Centaur were positive in 36/40 (90%). In children with CM allergy, SPT were positive in 17/22 cases (77.2%), sIgE CAP system in 25/27 (92.6%), and sIgE ADVIA Centaur system in 22/27 (81.5%). The mean age of children with CM allergy was 37.6 months, while the mean age of the children showing only sensitization to CM was 71 months. The mean age of children suffering from HE allergy was 33.7 months, while the age of sensitized children, without symptoms, was 45 months.

The diagnosis of respiratory allergy was evaluated in 30 cases for dust mites, in 10 cases for cat dander, and 49 cases for grass pollen. SPT were positive in 20 out of 22 children (90.9%) with dust mite allergy, sIgE CAP (at least one of the two allergens) in 28/30 (93.3%), and sIgE Centaur (at least one of the two allergens) in 26/30 (86.6%).

SPT were positive in 40/41 (97.6%) children with grass allergy; sIgE CAP (at least one of the two

Table 1. Performance of single tests: sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for skin prick tests (SPT), UniCAP sIgE (≥ 0.35 kU/l), and Centaur sIgE (≥ 0.35 kU/l) in allergic children.

	SPT	UniCAP	Centaur
Cow's milk ($n = 22$)			
Sensitivity (%)	77	91	82
Specificity (%)	88	70	74
PPV (%)	63	44	45
NPV (%)	94	97	94
Prevalence (%)	25	42	37
Hen's egg ($n = 34$)			
Sensitivity (%)	91	94	88
Specificity (%)	77	64	52
PPV (%)	65	55	46
NPV (%)	95	96	90
Prevalence (%)	44	54	60
Grass ($n = 41$)			
Sensitivity (%)	97	100	95
Specificity (%)	79	73	79
PPV (%)	58	64	68
NPV (%)	98	100	97
Prevalence (%)	45	50	44
Dust Mites ($n = 22$)			
Sensitivity (%)	91	91	86
Specificity (%)	76	62	64
PPV (%)	48	37	37
NPV (%)	97	97	95
Prevalence (%)	36	47	45
Cat ($n = 9$)			
Sensitivity (%)	100	100	100
Specificity (%)	81	71	70
PPV (%)	33	25	24
NPV (%)	100	100	100
Prevalence (%)	25	34	35

allergens) in 49/49 (100%), and sIgE Centaur (at least one of the two allergens) in 47/49 (95.9%). In children with cat allergy, all three tests showed positive results in 100% of cases. The mean age of those with mite allergy was 93 months, of those with grass pollen allergy was 98 months, and of those with cat allergy was 107 months.

Performance of allergometric tests

Statistical analysis of the three tests compared to allergic clinical diagnosis are reported in Table 1, but because some children did not undergo SPT, only those who were tested via all three methods are recorded.

The presence of IgE sensitization against CM and HE allergens was reported in about one-third of children with a slightly, but not significant, higher value for the *in vitro* tests with respect to SPT. The same percentage of sensitization in the two *in vitro* tests was observed against inhalant allergens.

The values obtained in the three tests for sensitivity, specificity, positive predictive value, and negative predictive value, are reported in Table 1. The percentage of sensitivity and specificity in subjects with clinical allergy was very similar; no statistically significant difference was observed between the UniCAP and ADVIA Centaur systems.

Table 2 shows the geometric mean of sIgE in allergic children and in sensitized children. The mean value in the sensitized ones is significantly lower than in those with clinical allergy in the UniCAP method; the ADVIA Centaur immunoassay shows a similar trend, with the exclusion of cow milk and *D. farinae* allergens: the mean value of sIgE is higher in sensitized children than in symptomatic ones (mean sIgE value for milk-sensitized children 3.1 kU/l vs. 0.8 kU/l; mean sIgE value for *D. farinae* 8.1 kU/l vs. 4.8 kU/l).

The correlation coefficients of the values of allergen-specific IgE measured by the UniCAP and Centaur systems for every allergen are presented in Figs 3–9.

Considering each different allergen separately, the percentages of patients positive to the UniCAP system or to the ADVIA Centaur immunoassay system, in relation to allergic children, are as follows: *C. dactylon*: UniCAP, 46 positive/49 allergic = 94%; ADVIA Centaur, 42 positive/49 allergic = 86%; *P. pratense*: UniCAP, 49 positive/49 allergic = 100%; ADVIA Centaur, 46 positive/49 allergic = 94%; *D. farinae*: UniCAP, 29 positive/30 allergic = 97%; ADVIA Centaur, 26 positive/

Table 2. Geometric mean of specific IgE (kU/l) in subjects with clinical allergy symptoms and in sensitized subjects.

						<i>Dermatophagoides</i>	
				<i>Cynodon dactylon</i>	<i>Phleum pratense</i>	<i>pteronyssinus</i>	<i>farinae</i>
	Cow's milk	Hen's egg	Cat				
Subjects with clinical allergy							
UniCAP	3.4*†	2.9*	14.8*	6.1*‡	15.3*	9.6*	6
Centaur	0.8†	3.4**	20.9*	2.7*‡	6.7**	11.3*	4.8
Sensitized without related symptoms							
UniCAP	1.6*‡	1.3*	2.3*	2.1*	3.1*	2.0*	5.2
Centaur	3.1‡	2.4**	2.2*	1.8*	4.3**	2.1*	8.1

* P value < 0.001 for allergic vs. sensitized patients.

** P value < 0.05 for allergic vs. sensitized patients.

† P value < 0.01 UniCAP vs. Centaur.

‡ P value < 0.05 UniCAP vs. Centaur.

30 allergic = 87%; *D. pteronyssinus*: UniCAP, 29 positive/30 allergic = 97%; ADVIA Centaur, 25 positive/30 allergic = 83%.

Discussion

Evidence for specific sensitization can be obtained by *in vivo* or *in vitro* tests. Any assay for the IgE antibody

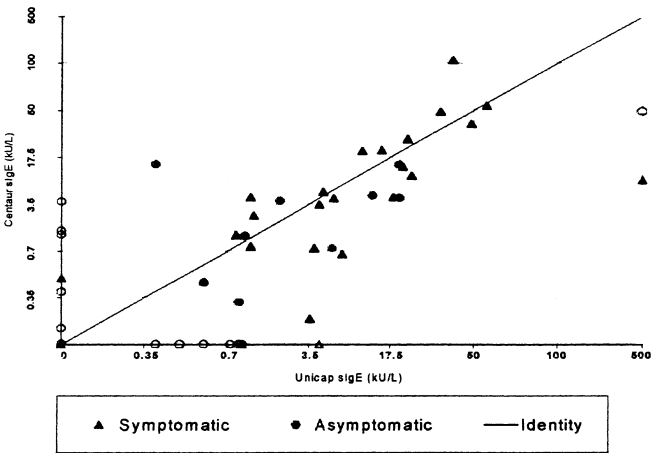


Figure 3. Centaur sIgE vs. UniCAP sIgE for *Dermatophagoides farinae* d1. Correlation coefficients for symptomatic patients 0.608, asymptomatic 0.493, all 0.631; number of samples for symptomatic patients 25, asymptomatic 26, all 51. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

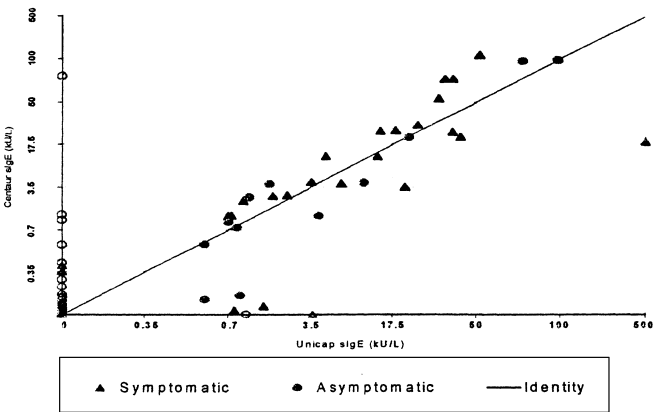


Figure 4. Centaur sIgE vs. UniCAP sIgE for *Dermatophagoides pteronyssinus* d2. Correlation coefficients for symptomatic patients 0.78, asymptomatic 0.711, all 0.790; number of samples for symptomatic patients 26, asymptomatic 31, all 57. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

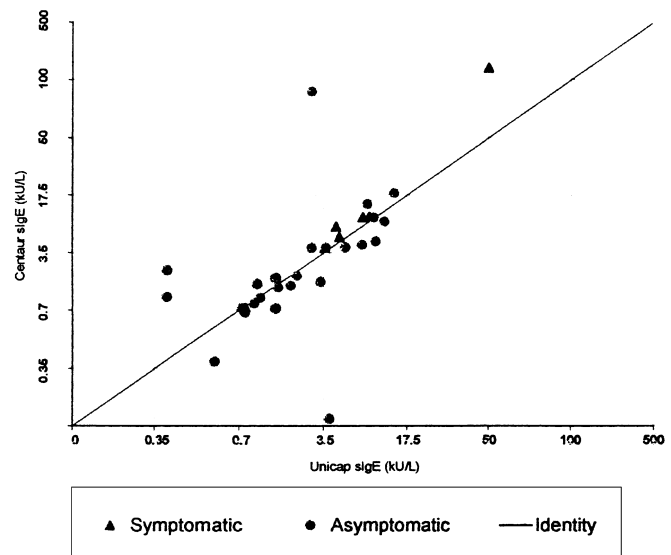


Figure 5. Centaur sIgE vs. UniCAP sIgE for cat dander e1. Correlation coefficients for symptomatic patients 0.921, asymptomatic 0.371, all 0.564; number of samples for symptomatic patients 7, asymptomatic 26, all 33. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

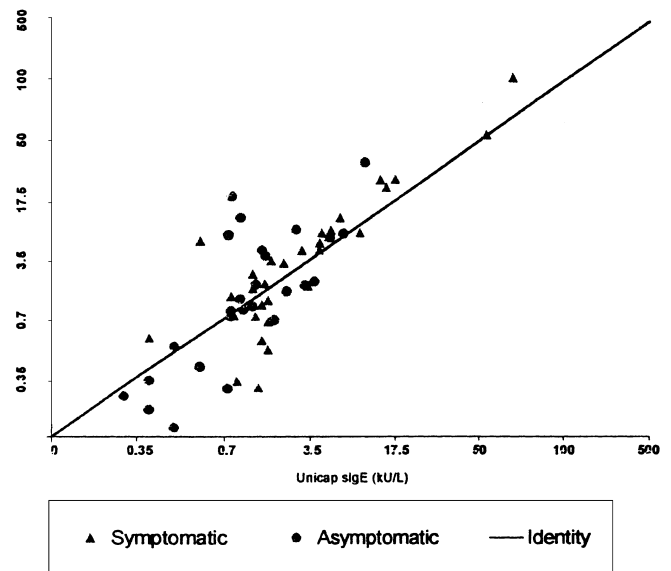


Figure 6. Centaur sIgE vs. UniCAP sIgE for hen's egg f 8. Correlation coefficients for symptomatic patients 0.791, asymptomatic 0.720, all 0.771; number of samples for symptomatic patients 31, asymptomatic 26, all 57. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

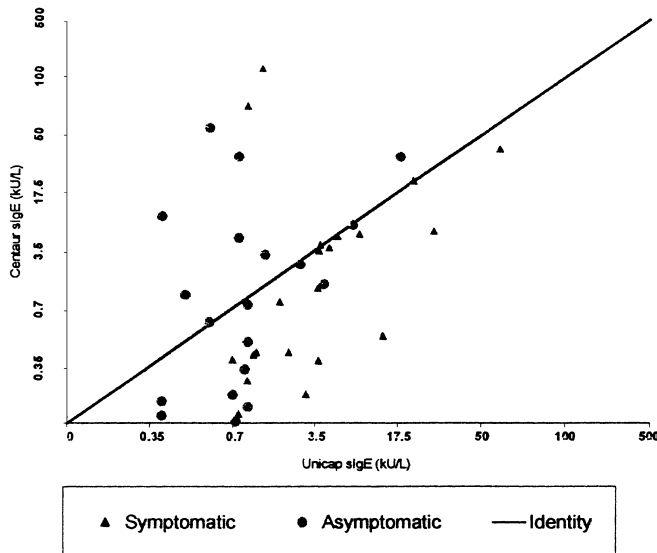


Figure 7. Centaur sIgE vs. UniCAP sIgE for cow's milk f2. Correlation coefficients for symptomatic patients 0.406, asymptomatic 0.309, all 0.379; number of samples for symptomatic patients 21, asymptomatic 19, all 40. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

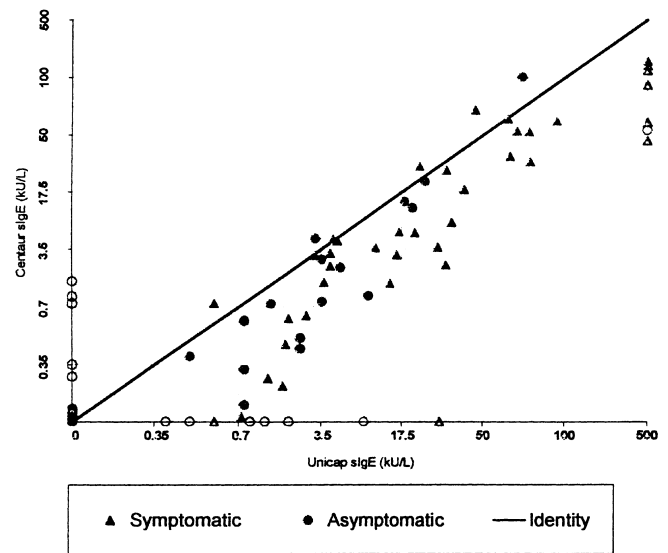


Figure 9. Centaur sIgE vs. UniCAP sIgE for *Phleum pratense* g6. Correlation coefficients for symptomatic patients 0.871, asymptomatic 0.822, all 0.907; number of samples for symptomatic patients 41, asymptomatic 100, all 141. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

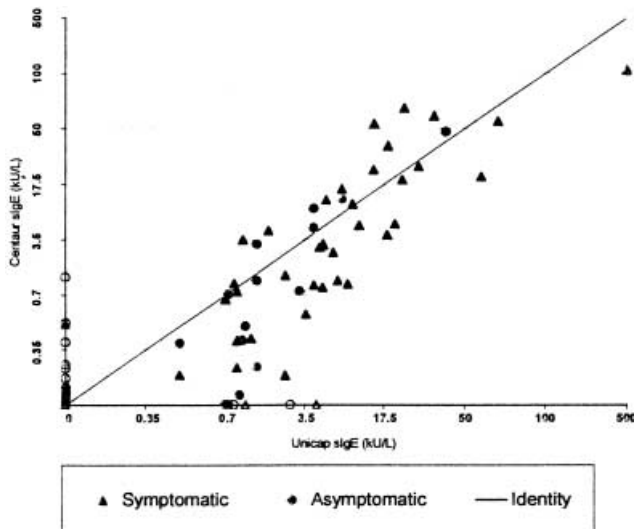


Figure 8. Centaur sIgE vs. UniCAP sIgE for *Cynodon dactylon* g2. Correlation coefficients for symptomatic patients 0.803, asymptomatic 0.796, all 0.881; number of samples for symptomatic patients 41, asymptomatic 100, all 141. Centaur samples (solid marker) have numerical values for both the Centaur and UniCAP systems. Flagged samples (open marker) Centaur < 0 and UniCAP < 0.35 plotted at 0 Centaur > 500 and UniCAP > 100 plotted at 500.

should be specific, should show no cross-reactivity with IgG, and not experience interference due to the presence of high total IgE (2, 3). Results of testing surveys suggest that not all *in vitro* tests for specific IgE show similar results (6, 7). We have chosen to compare a new method (ADVIA Centaur immunoassay system sIgE assay) with our current method (UniCAP FEIA system) that is considered a standard reference—as demonstrated in a recent study also (7). The “architecture” of the ADVIA Centaur eliminates competition between allergen-specific IgE and allergen-specific non-IgE antibodies of different isotypes, and increases the selectivity of the IgE class antibodies. The concentration of the biotinylated allergen enables the assay to adjust detection of antibodies based on affinity, thereby excluding responses from low-affinity polyreactive IgE immunoglobulins. This study analyzes the performances of the tests in a routine group of children, with different allergic diseases at various grades of severity, in relation to the most frequent causative allergens. No difference in the value of sIgE can be found if the serum sample is stored at -20°C , as reported previously (8).

Food allergy was observed in most of the children affected by atopic dermatitis. Because pathogenesis of food allergy in atopic dermatitis is bound to different immunological mechanisms—not only IgE-mediated ones—no test is 100% accurate for the diagnosis of food allergy. That said, the gold standard for testing for food allergy is clinical challenge (provocation testing) (9–12).

In our study, the food challenge for CM and HE allergy identified 27 and 40 cases, respectively. The results obtained in the children by *in vivo* and *in vitro* tests, compared to food challenge, are in keeping with those observed recently by other authors. In subjects with milk allergy, Vanto et al. (9) reported sensitivity for SPT of 69%, and 58% for sIgE, with a specificity of 91% for SPT, and 88% for sIgE. The study by Majamaa et al. (10) in infants with cow's milk allergy reported values with a higher specificity (98% for SPT and 94% for sIgE) but with lower sensitivity (14% for SPT and 26% for sIgE). Roehr et al. (11) reported in subjects with milk allergy a sensitivity of 78% for SPT and of 84% for sIgE; the same authors reported in children with egg allergy a sensitivity of 89% for SPT, 96% for sIgE, and specificity of 57% for SPT, 36% for sIgE.

The diagnosis of respiratory allergy was obtained in children when there was the presence of a strong link between history, presence of symptoms when allergen exposure occurs, and positive allergometric tests (*in vivo* and/or *in vitro*). In children with cat allergy, we showed the same percentage of sensitivity for *in vivo* and *in vitro* tests, while for grass pollen and dust mite allergies the UniCAP system performed slightly better, though the difference was not statistically significant.

The detection of specific IgE antibodies establishes that sensitization has occurred, and does not always indicate the presence of an allergic disease (12,13). An early food allergy is often followed by sensitization to common environmental allergens, and sensitization to aeroallergens usually precedes symptomatic inhalant allergies by several years (11,14,15). Sometimes food sensitization also persists, in children with AEDS, even though food tolerance has been reached. The geometric mean of specific IgE concentration (Table 2) shows that the values of both *in vitro* tests is higher for allergic patients than for sensitized ones, as we expected, with the exception of CM and *D. farinae* allergens for the ADVIA Centaur system. The level of specific IgE has often been used as a quantitative measure for reactivity to various allergens (16). Attempts have been made to define the concentration of antibody that can, with a specified degree of probability, predict reactivity to a certain allergen (16). However, it is difficult to comment on patients with sensitization only, because in the absence of clinical symptoms it is difficult to determine what is the reference

point. In children, mostly with AEDS, a positive reaction specific for pollen or mites may be present without apparent clinical symptoms. Specific IgE values obtained with the ADVIA Centaur system showed good correlation (Figs 3–9) with those of the UniCAP system in symptomatic people allergic to hen's egg, dust mites, grass pollen, and cat allergens, while such correlation was low in asymptomatic cases for inhalant allergen and mites and in children with cow's milk allergy (Fig. 7).

Demonstrating the presence of specific IgE constitutes an essential part of the diagnosis of allergic diseases and improved technology gives more relevance to *in vitro* tests. The evaluation of IgE sensitization is also relevant in relation for monitoring changes in a patient's response to allergen avoidance, or as a predictive value in evaluation of the response to a food challenge, or for the appearance of allergic respiratory sensitization. The advantages of the ADVIA Centaur immunoassay system, if our data are confirmed by other observations and with other allergens, may be numerous: small sample size (25 µl per allergen vs. 40 µl for the UniCAP system, which is key for pediatric testing); rapid turnaround time; complete automation (hands-on time 10 min for Centaur vs. 1.5 h for UniCAP); and no interference from IgG (17).

Another advantage, yet to be fully appreciated, is the assay's unique calibration method. At present, there is no single industry-wide method for calibrating specific IgE assays. The two most common calibration schemes—heterologous interpolation and homologous interpolation—have limitations. The ADVIA Centaur assays do not incorporate either of those calibration schemes. Instead, the Centaur assays are the only commercially available ones using the latest calibration technology—a recombinant allergen in combination with specific human IgE antibodies. This calibration technology delivers a truly quantitative calibration against the total IgE WHO reference. So while it may currently contribute to discrepancies among competitive assays, it is difficult to dispute its quantitative results.

The ADVIA Centaur also offers many other beneficial features that were not used in this study, but that are key to improving productivity and decreasing overall costs for the laboratory. These include the integration of allergy testing into routine immunoassay testing (assays can be run in random access with each other and all other immunoassays) and reflex testing in random access.

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