

Quantitative IgE antibody assays in allergic diseases

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During the past several years, immunoassays for specific IgE antibodies have been refined to permit reporting results in mass units. Thus quantitative immunoassays for IgE antibodies may be an adjunct to skin tests. In cases of food allergy among children with atopic dermatitis, cutoff values for IgE antibody concentrations to egg, milk, peanut, and fish have been derived to provide 95% positive and 90% negative predictive values. Food-specific IgE antibody determinations can also be used to predict which food allergies are resolving spontaneously. Elevated egg-specific IgE antibody levels in infancy are associated with significantly increased risk for development of inhalant allergies later in childhood. In cases of inhalant allergy, specific IgE antibody levels correlate closely with results of inhalation challenge studies in cat-sensitive persons. Also, mite-specific IgE antibody levels correlate significantly with the mite allergen contents of reservoir dust in the homes of mite-sensitive persons. Immunoassays for quantitation of specific IgE antibodies may be used to document aller-

gen sensitization over time and to evaluate the risk of reaction on allergen exposure. However, immunoassays and skin tests are not entirely interchangeable, and neither will replace the other in appropriate circumstances. (*J Allergy Clin Immunol* 2000;105:1077-84.)

Key words: IgE antibody, quantitative immunoassay, allergic disease

Since the discovery of IgE more than 30 years ago and the subsequent establishment of immunoassays for allergen-specific IgE antibodies, many controversies have arisen. Initial debates centered on the relative sensitivity and specificity of those immunoassays versus skin testing, as well as on the various methods used for reporting immunoassay results. In particular, the cutoff point used to separate normal from elevated IgE antibody levels has been a persistent issue. In recent years the immunoassays have undergone several refinements, including the substitution of enzyme-tagged monoclonal detection antibodies for the original radiolabeled polyclonal antibodies; the development of solid-phase support systems with higher allergen binding capacities; and the introduction of an assay system in which fluid-phase allergen is bound to the solid phase only after the allergen has complexed with fluid-phase IgE antibodies. Although older assays are still available, newer immunoassays have the capacity to quantitate IgE antibodies in mass units, and the clinical significance of such quantitation is being studied. The current article summarizes a workshop regarding the technical and clinical benefits of these improved immunoassays.

MEASUREMENT OF IgE ANTIBODY IN MASS UNITS Immunoassay design

Allergen-specific IgE antibodies are measured in the presence of other antibodies of the same isotype and antibodies of other isotypes specific for the same allergen. This requires specific recognition by the allergen-binding sites (Fab) and the isotype-specific epitopes (Fc) in the same

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Abbreviations used

FDA:	US Food and Drug Administration
ID:	Intradermal (skin test)
kU/L:	Kilounits per liter
kU _A /L:	Kilounits of antibody per liter
NPV:	Negative predictive value
PPV:	Positive predictive value
SPT:	Skin prick test
WHO:	World Health Organization

assay. All assay designs therefore include a solid phase for the separation of bound and unbound IgE antibodies. The allergen source materials used in the assay should be well characterized, and critical allergens should not be lost during the production of reagents; this provides precise and reproducible data in clinical allergy investigations.¹

An assay that provides a large excess of major and minor allergens maximizes the binding of IgE antibodies. This makes the assay less easily inhibited by competing antibodies of other isotypes. It also provides conditions for quantitation of the sum of all bound antibodies on the basis of their specificity in an affinity-independent manner. The law of mass action, applied to heterogeneous solid-phase immunoassays, predicts that when the available allergen concentration is increased to the level where 90% of the IgE antibody of the serum sample is bound to the solid phase, the assay is essentially independent of the affinity between each IgE antibody and its epitope.²

Anti-IgE preparations must be IgE Fc specific. First-generation assays used affinity chromatography-purified polyclonal antibodies, whereas newer assays use mixtures of polyclonal and monoclonal antibodies with complementary dose-response characteristics. This ensures greater assay precision over time.

Quantitative immunoassays for specific IgE antibodies require the inclusion of a standard curve. Calibrators for both specific and total IgE measurements should be traceable to the World Health Organization (WHO) International Reference Preparation for Human IgE, 75/502. If the solid-phase allergen is present in excess and has the capacity to bind the IgE antibodies quantitatively over the whole range of concentrations, this permits demonstration of parallelism between the different samples and the calibrator curve even above this range.^{3,4} An example showing measurement of total IgE and specific IgE in serially diluted samples is shown in Fig 1.⁵ Model experiments have confirmed that the allergen-specific IgE unit (kU_A/L) is equal to the international unit (kU/L) for IgE protein.⁵

Quantitation of IgE antibodies: Quality assurance and quality control

Quality assurance and quality control encompass all those measures taken to guarantee that the assay will perform in a reliable fashion. Quality assurance by manufacturers includes specifications for all phases of production to verify that a reagent is performing according to

specifications. Before licensing a product, the US Food and Drug Administration (FDA) requires that these elements are in place.

Manufacturers of allergen extracts have relatively simpler requirements for quality assurance because these extracts are considered biologic products rather than test devices. During the past decade several allergens commonly used in the United States have been standardized, including extracts of house dust mites, *Hymenoptera* venoms, cat hair/dander, short ragweed pollen, and several grass pollens. Standardized extracts contain defined quantities of major allergens or are labeled in units that correlate with biologic activity. Also, allergenic extracts are required to be sterile and labeled with expiration dates that reflect both the time of manufacture and the diluent being used.

Test devices for specific IgE come under different regulations that include proof of safety. For the manufacturers, this requires calibration of equipment, characterization of allergen reagents, documentation that reagents are specific, assessment of interlot and intralot reproducibility, and submission of this information with each new lot of test materials produced.

Significant improvements have been achieved in the performance of tests for IgE antibodies by clinical laboratories. In addition to the improvements in the test systems described above and in technology used by clinical laboratories, much attention has been focused on the laboratories themselves. The Clinical Laboratory Improvement Amendments of 1988 set standards for all laboratories engaged in clinical testing.⁶ These standards include requirements for trained supervisory and testing personnel, record keeping and instrument maintenance, daily quality control practices, result reporting, and laboratory inspection and accreditation. In addition, specific recommendations for performing tests for IgE antibodies are detailed in a recent publication from the National Committee for Clinical Laboratory Standards.⁷ The recommendations include quality control procedures for daily performance of tests in the clinical laboratory setting and minimal performance targets for IgE antibody assays. For example, interassay coefficient of variation in IgE antibody assays should not exceed 15%. Clinical laboratories are also encouraged to participate in a program of interlaboratory proficiency testing. Such programs are available from some manufacturers of reagent test systems⁸ and from independent providers, such as the College of American Pathologists. Proficiency testing provides a benchmark of accuracy for results reported by clinical laboratories. The results also enable laboratories to assess their own performance and the performance of various commercially available testing systems. With respect to quantitation of IgE antibodies, the results of proficiency testing indicate that some, but not all, clinical laboratories report results for sera that contain IgE antibodies to several common allergens with interlaboratory coefficients of variation of less than 15%.⁹ However, proficiency testing has not been performed with all available allergens. Clinicians should be alert to the performance

of their own laboratories and should ask the laboratory director about the type of test procedure in use and its performance on proficiency test specimens.

Quantitative IgE levels for predicting development of atopic disorders

Prompt perinatal identification of high-risk atopic infants is important to institute preventive efforts early in life because a critical period exists early postnatally in which the genetically programmed atopic-prone infant may be at an increased risk to become sensitized to allergens. Unfortunately, there does not exist today any prenatal atopic marker with a high enough predictive capacity to be practical for screening for the high-risk infant. An elevated cord blood IgE level may be useful for identifying high-risk children for research purposes.¹⁰ Alternatively, high-risk infants could be identified for allergy prevention after the development of an indicator atopic marker, such as a food- or aeroallergen-specific IgE antibody level.

Ease and accuracy of measurement is important for a screening test. The prevalence of the atopic marker in the population screened will affect the sensitivity of the screening test; the lower the prevalence, the lower the sensitivity. The time of onset of the marker is important; the earlier the onset, the greater likelihood that the test will be clinically meaningful.

Early sensitization to chicken egg has been evaluated as a marker for development of atopic disease. Detectable egg white-specific IgE (≥ 0.35 kU_A/L) at age 8 months (9% prevalence) in an unselected cohort of 86 Swedish girls evidenced 50% sensitivity, 97% specificity, and 70% positive predictive value (PPV) for atopy at 7 years, which was a better predictor than was elevated cord blood IgE levels among the same cohort (Table I).¹¹ Similarly, a positive ovalbumin SPT at age 6 months showed a 40% sensitivity and 95% specificity for atopic disease at age 18 months.¹⁷ Elevated egg-specific IgE (≥ 0.35 kU_A/L) by age 1 year in an unselected birth cohort is associated with a significant increase in both outdoor and indoor aeroallergen sensitization by age 3 years (Table I).¹² Increasing the cutoff value of egg-specific IgE to ≥ 2 kU_A/L increased the PPV to about 75% but lowered the sensitivity to about 15%. However, only 3% of the cohort had levels of egg-specific IgE ≥ 2 kU_A/L compared with 10% having levels ≥ 0.35 kU_A/L.

In two high-risk birth cohorts Burr et al¹⁴ and Zeiger and Heller¹³ observed that a positive egg SPT by age 1 year (7%-15% prevalence, respectively) evidenced moderate PPV (48%) for mite sensitization to high PPV (>70%) for outdoor and indoor aeroallergen sensitization and allergic rhinitis or allergic asthma. Sensitivities for these tests were unfortunately extremely low (20%-30%), but specificities were high (>90%). The prevalence of allergic rhinitis and aeroallergen sensitization were increased by at least a 2-fold factor in these high-risk infants with positive egg SPTs.^{13,14}

Elevated IgE antibody concentrations (≥ 0.35 kU_A/L) to one of four food allergens (egg, milk, soy, or wheat) at

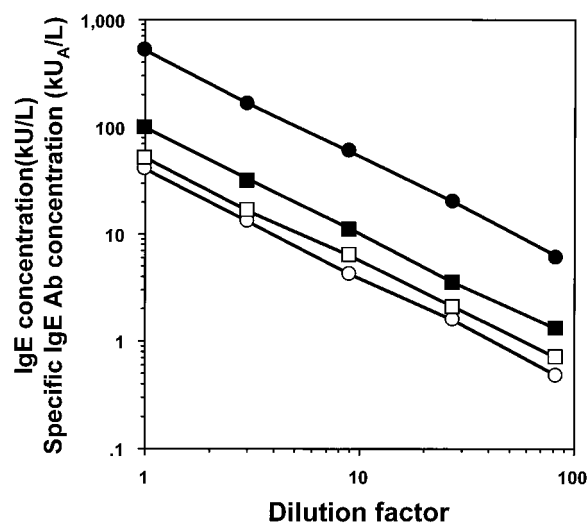


FIG 1. Parallelism of sample and calibrator dilutions demonstrated by measurement of total (closed symbols) and allergen-specific (open symbols) IgE in serial 3-fold dilutions of two sera (squares, circles) containing different quantities of birch pollen-specific IgE antibodies.⁵

age 1 year (14% of a birth cohort of 165 infants) evidenced high PPV and specificity but low sensitivity for aeroallergen sensitization at age 5 years ($P < .001$) (Table I).¹⁵ A persistently elevated food-specific IgE antibody (≥ 0.35 kU_A/L) by 2 years of age showed a significant predictive capacity for allergic rhinitis and asthma at age 5 years ($P < .001$) (Table I).¹⁶ However, screening at age 2 years for persistent food sensitization delays identification of high-risk children and postpones initiation of preventive measures.

Meta-analyses of epidemiologic studies have quantified the modifiable risk factors for asthma. Parental smoking, breast-feeding for less than 3 months, and consumption of a low fish/omega-3 diet, all reported as risk factors for asthma, account for only 1.3-, 1.5-, and 1.7-fold risks, respectively.¹⁸ Conversely, mite sensitization early in infancy accounts for 3.4-fold and 19.7-fold risks with low level and high level exposure, respectively.¹⁸ Thus efforts to reduce mite exposure levels are paramount for effective asthma prevention. Recent studies that have effectively reduced mite exposure by physical means (antimite bedding encasements, residence at high altitudes) have shown a significant effect in preventing mite sensitization¹⁹ or development of symptoms in persons already sensitized to mites²⁰ and in reducing mite-specific IgE concentrations in sensitized and symptomatic mite-sensitive persons.^{21,22} These encouraging results need to be confirmed in larger multicenter trials. Should such large-scale trials confirm the effectiveness of mite avoidance methods to suppress mite-specific IgE, then identification of the high-risk child becomes paramount for introduction of secondary and tertiary allergy prevention.

TABLE I. Capacity of food sensitization in infancy and early childhood to predict the development of inhalant sensitization, allergic rhinitis, and asthma from ages 3 to 7 years in unselected and high-risk cohorts

Study	Cohort	Risk factor (prevalence %)	Outcome (prevalence %)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Statistical significance
Hattevig et al ¹¹	Unselected females (n = 86)	8-mo egg-IgE ≥ 0.35 kU _A /L (9%)	7-y + inhalant-IgE (11%)	56	96	63	95	$P < .001$
Nickel et al ¹²	Unselected (n = 434)	1-y egg-IgE ≥ 0.35 kU _A /L (10%)	7-y atopy (15%) 3-y outdoor allergen-IgE ≥ 0.35 kU _A /L (10%)	50 20	97 93	70 36	92 93	$P < .001$ $P < .001$
Zeiger and Heller ¹³	High-risk (n = 165)	≤ 1 -y + egg SPT (16%)	7-y + inhalant SPT (45%) 7-y allergic rhinitis (39%) 7-y asthma (31%)	24 28 24	92 93 88	72 72 48	58 65 72	$P < .001$ $P < .001$ $P = .046$
Burr et al ¹⁴	High-risk (n = 427)	6-mo + egg SPT (7%)	7-y + mite SPT (19%)	20	96	48	83	$P < .001$
Kulig et al ¹⁵	Unselected (n = 165)	1-y + food-IgE (egg, milk, wheat, or soy) ≥ 0.35 kU _A /L (14%)	5-y mite-IgE ≥ 0.35 kU _A /L (30%)	35	94	71	77	$P < .001$
Kulig et al ¹⁶	Unselected (n = 459)	≤ 2 -y persistent food-IgE ≥ 0.35 kU _A /L (10%)	5-y allergic rhinitis (18%) 5-y asthma (9%)	24 40	93 93	44 36	93 94	$P < .001$ $P < .001$

TABLE II. PPV and NPV of food-specific IgE concentrations (kU_A/L) for predicting reactions on oral challenge of children and adolescents with atopic dermatitis²⁵

	>95% PPV	>90% PPV	>95% NPV	>90% NPV
Egg	6	2	—	0.6
Milk	32	23	0.8	1.0
Peanut	15	9	Best NPV = 85% at <0.35 kU _A /L	
Fish	20	9.5	0.9	5
Soy	Best PPV = 50% at 65 kU _A /L		2	5
Wheat	Best PPV = 75% at 100 kU _A /L		5	79

There was no relationship between IgE antibody level and severity of the reaction.

Quantitative IgE levels in food allergy

Earlier studies suggested that quantitative tests for food-specific IgE might assist clinicians in establishing the clinical relevance of food sensitization and in following patients over time for development of tolerance.^{23,24} In a subsequent study Sampson and Ho²⁵ studied 196 children and adolescents (mean age 5.2 years, 60% male) with atopic dermatitis who were randomly selected from a pool of 300 patients who underwent evaluation for food allergy over a 10-year period. Stored sera were analyzed for specific IgE antibodies to foods commonly causing allergy in children, including egg, milk, peanut, soy, wheat, and fish. Food allergy was diagnosed by double-blind, placebo-controlled oral food challenges or by a "convincing" history of anaphylactic reactions. The prevalence of specific food

allergies in the group ranged from 22% for wheat to 73% for egg. The performance characteristics of SPTs (positive response = wheal ≥ 3 mm than the negative control) and the quantitative immunoassay (positive response = ≥ 0.35 kU_A/L) (egg, milk, peanut, fish) were comparable, with excellent sensitivity and negative predictive accuracy but poor specificity and positive predictive accuracy. Diagnostic concentrations of food-specific IgE antibodies indicating 95% and 90% PPV and negative predictive value (NPV), respectively, were derived, as shown in Table II. In our experience, the use of these cutoff values as decision points for performing oral food challenges can reduce the need for oral challenges by about 50%. The poor predictive values for soy and wheat are presumably due to cross-reacting proteins between these foods and peanut and grass pollen, respectively.

TABLE III. A comparison of the performance characteristics of various diagnostic tests for cat-induced asthma³¹

Diagnostic test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Efficiency (%)
SPT					
FEV ₁	96.9 (±3.8)	80.9 (±8.6)	78.5 (±9.0)	97.4 (±3.5)	87.5 (±7.2)
Any +	79.2 (±8.9)	90.6 (±6.4)	92.6 (±5.7)	74.3 (±9.6)	83.4 (±8.2)
ID skin testing					
FEV ₁	0	31.6 (±14.6)	0	92.3 (±8.4)	30.8 (±14.5)
Any +	60.0 (±15.3)	31.0 (±14.5)	23.1 (±13.2)	69.2 (±14.5)	38.5 (±15.3)
Cat-specific IgE antibody assay					
FEV ₁	90.9 (±6.6)	84.1 (±8.3)	74.1 (±9.9)	94.9 (±5.0)	86.4 (±7.1)
Any +	69.2 (±10.5)	100	100	72.7 (±10.1)	83.1 (±8.5)

The sensitivity, specificity, PPV, NPV, and efficiency of SPTs, ID skin tests, and cat-specific IgE antibody assays are displayed with regard to the maximum decline in FEV₁ and any positive challenge outcome (Any +), with 95% confidence limits indicated in parentheses.

Crespo et al²⁶ also investigated the use of quantitative IgE antibodies for the prediction of acute reactions to eggs. Forty children with acute reactions to chicken egg, but without atopic dermatitis, were challenged orally to egg after 2.5 years of egg elimination. The results of oral challenges were correlated with the concentration of egg-specific IgE antibody at the time of the challenge. The likelihood ratios for a positive oral challenge (egg white IgE level ≥ 0.35 , 0.70, and 1.20 kU_A/L) were 2.2, 3.0, and 6.3, respectively. In a study of children with acute allergic reactions to peanut, walnut, or pecan,²⁷ children with acute reactions had concentrations of food-specific IgE antibody that were significantly higher than children who could tolerate these foods.

Monitoring the concentration of specific IgE antibody to foods such as milk, egg, soy, and wheat holds promise for monitoring dietary avoidance and for predicting when clinical tolerance will develop. Strict elimination of the causal food can lead to improvement in children with atopic dermatitis.²⁸ Elimination of egg in egg-sensitive persons with atopic dermatitis was associated with improved skin symptoms and a decline in egg-specific IgE antibody²⁹; when the food was not eliminated, no such decline was observed. Finally, children with confirmed milk allergy who were destined to outgrow their milk allergy had a lower concentration of milk-specific IgE antibody than did those who maintained their reactivity into late childhood (median 4 vs 78 kU_A/L).³⁰

Quantitative IgE antibody levels in inhalant allergy

Just as the quantitation of food allergen-specific IgE levels can be used to guide dietary restrictions in persons with food allergy, specific IgE levels to some inhalant allergens can be used to guide environmental control measures for persons with respiratory allergy. There are three lines of evidence to support this observation: that these assays are accurate markers of allergic sensitization, that specific IgE levels are related to allergen exposure, and that allergen avoidance can lead to a reduction in specific IgE levels.

First, it is clear that quantitative IgE levels to inhalant allergens are an accurate measure of individual patient

sensitivities. In a recent study by Wood et al,³¹ cat-specific IgE antibodies were shown to be overall equal to SPTs and superior to intradermal (ID) skin tests in the diagnosis of clinical reactivity to cat allergen (Table III). All subjects with elevated IgE antibodies had at least one positive challenge outcome compared with only 12 of 44 subjects without measurable cat-specific IgE antibodies. In addition, no subject with a negative SPT, including those with a positive ID skin test, had elevated cat-specific IgE antibodies. When data were analyzed with regard to any positive challenge outcome, the specific IgE antibody assay had a sensitivity of 69%, a specificity of 100%, a PPV of 100%, and an NPV of 73%.

Second, at least with regard to house dust mite, it has been shown that specific IgE levels may serve as a marker of current allergen exposure as well as sensitivity. In a study of 40 mite-sensitive persons, De Lovinfosse et al³² found a high degree of correlation between the concentrations of mite-specific IgE and the concentration of mite allergen in mattress dust ($P = .001$). Subjects with an IgE antibody concentration of >2 kU_A/L had a 77% probability of being exposed to a high level of mite allergen (>10 μ g/g dust), whereas subjects with IgE antibody concentrations <2 kU_A/L had a 77% chance of being exposed to a mite allergen level of <10 μ g/g dust. These data are particularly important in that they may allow the clinician to identify not just patients with mite sensitivity but also those who are most in need of environmental control measures.

Third, several studies have shown that allergen-specific IgE antibody concentrations may decline after allergen avoidance measures have been instituted. For example, median levels of specific IgE to *Dermatophagoides pteronyssinus* declined to 89 kU_A/L from 117 kU_A/L in 18 mite-sensitive children after 3 months of residence at a mite-free (<2 μ g group I antigen/g dust) boarding school in the Italian Alps.²¹

This evidence clearly supports the use of IgE antibody assays for the common inhalant allergens and strongly suggests that SPTs and quantitative immunoassays have comparable sensitivity. For other allergens the situation may be more complex, and in particular for some fungi the relationships may be different. In general, it is diffi-

cult to establish that a given patient's symptoms are specifically related to a given fungus (eg, *Alternaria*). However, skin tests and specific IgE antibody assays have been shown to predict symptoms.^{33,34} For other fungi, the relationship between extracts used for skin testing and those used for immunoassays is less well defined. These differences may be quantitative or qualitative.³⁵ There is clearly a need for further research on fungal allergens and on improving the standardization of methods used to determine sensitization to fungi.

Specific uses of quantitative IgE antibody assays in other allergen systems

As discussed previously, quantitative information about food-specific IgE levels may reduce the need for additional testing, such as a food challenge. Whether quantitation of allergen-specific IgE antibodies can improve the management of allergy to natural rubber latex, *Hymenoptera* venom, drugs, or other allergens remains to be determined.

Several recent studies have investigated the utility of quantitating IgE antibodies in latex allergy. In persons with spina bifida at risk for latex allergy, Bernardini et al³⁶ found that a latex-specific IgE concentration of >3.5 kU_A/L was highly predictive for symptomatic sensitivity. In occupational settings, could measurements of latex-specific IgE be used to assess the adequacy of allergen avoidance? Hamilton and Brown³⁷ presented information on a group of 11 anesthesiologists who began latex avoidance precautions after learning that they were sensitive to latex. After 15 months at work with latex precautions, the average level of latex-specific IgE in these individuals had declined from 2.8 ± 0.8 kU_A/L to 2.1 ± 0.9 kU_A/L ($P < .01$, Spearman rank test). These studies suggest that levels of specific IgE may decline with adequate allergen avoidance. However, much more information is needed before monitoring can be recommended as a routine clinical practice.

In studies of insect venom allergy,³⁸ and less so for β -lactam hypersensitivity,³⁹ highly sensitive in vitro assays for specific IgE approximate the sensitivity and specificity of SPTs. It would be valuable to learn whether the quantitation of IgE specific for venom or drug were predictive of symptomatic allergy for either of these allergens.

ARE SKIN TESTS AND IMMUNOASSAYS FOR SPECIFIC IgE INTERCHANGEABLE?

Skin tests are the original and still most widely used method for demonstrating IgE antibody in the United States. The reaction of the skin to the introduction of allergen extract is only in part determined by the levels of allergen-specific IgE antibody. In epidemiologic studies there is strong evidence that the reaction of the subject's skin to histamine is a strong contributor to the results of skin testing.⁴⁰

Many variables have been reported to affect the response to allergen skin testing, including season, time of day, and area of the body tested. The effect of most of

these variables is small and will affect the results only when the magnitude of skin test reactivity is low.

Another factor that will affect the results of skin tests independent of the underlying levels of specific IgE is the use of medications with antihistamine properties, including a number of antidepressants. The device used for the performance of the skin test will affect the results because of introduction of differing amounts of extract into the skin.⁴¹ The quality of extract used for skin testing will also introduce a variable in the results of skin testing; the same problem occurs with the specific IgE immunoassays.

The relative sensitivity of the skin test varies greatly between epicutaneous skin testing and ID testing. If the purpose of skin testing is to detect IgE-mediated sensitization, it is important to compare the performance of these two skin test methods. Prick skin testing with good quality allergy extracts has been shown to be positive in many individuals who have no clinical symptoms.^{42,43} ID testing in SPT-negative subjects has been shown in several studies to not correlate with clinical disease.^{31,44,45}

In studies in which the SPT was accepted as the gold standard, in vitro testing has proved less sensitive. Reported sensitivities have ranged from 74%⁴⁶ to 92.2%.⁴³ In the latter study sensitivity was greater (95.1%) in those with symptoms from the allergen compared with 88.7% in those who were asymptomatic but who had positive SPTs. The clinical significance of IgE antibodies demonstrated by either SPT or immunoassay must be determined by a physician who has taken a history and examined the patient.

If the sensitivity of immunoassays for specific IgE approaches that of the SPT as a diagnostic test, has allergy skin testing become obsolete? Clearly not, although perhaps considerations of practicality and cost will predominate. For example, the results of allergy skin tests are immediately available and inexpensive to perform. There is also at times a benefit in being able to demonstrate the skin reaction to a doubting patient (for example, allergy to a pet). On the other hand, for those not trained in allergy skin testing or for those wishing to perform comparative testing over time, the quantitative immunoassay offers definite advantages. There appears, however, to be one area where the two approaches are not interchangeable. Although the response to allergen immunotherapy is initially a rise in specific IgE followed by a gradual fall,⁴⁷ SPT positivity decreases rapidly as maintenance doses are achieved.⁴⁸ A decrease in the positivity of a titrated SPT is highly predictive of continued remission after cessation of allergen immunotherapy.⁴⁹ Thus in vitro and in vivo measurements of specific IgE antibodies are not entirely interchangeable, and neither will replace the other in appropriate circumstances.

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