Original Research

Predictive value of skin prick tests and radioallergosorbent tests for clinical allergy to dogs and cats

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The predictive value and post-test probability of disease were compared for skin prick tests and radioallergosorbent tests (RASTs) in 168 children suspected of clinical allergy to dogs and cats. The skin tests included negative and positive (histamine) controls. The results of RASTs with the same allergen extracts were expressed in relation to the results with allergen-specific pooled reference serum. All the tests were performed blind. The predictive values of positive test results were comparable and low (53% to 76%), whereas the predictive values of negative test results were comparable and high (88% to 95%). The post-test probability of clinical allergy to dog or cat allergen, based on the prevalence rates in the referral population (15.1% and 22.5% respectively), increased to between 46% and 67% for positive test results and decreased to between 4% and 8% for negative results, which suggests that the primary role of skin prick tests and RASTs is in eliminating the diagnosis of clinical allergy.

Chez 168 enfants soupçonnés cliniquement d'allergie aux chiens et aux chats, on compare le pouvoir de détection des cuti-réactions et de la recherche des IgE spécifiques (dite RAST). Les cuti-réactions sont assorties de témoins négatifs et positifs (ces derniers à l'histamine). Les résultats du RAST pour un extrait allergénique donné sont exprimés par rapport à la réaction obtenue à partir d'un sérum mélangé de référence, spécifique quant à cet allergène. Tous les examens sont pratiqués en respectant l'insu. On trouve pour les résultats positifs un pouvoir de détection comparable et bas (de 53% à 76%) et pour les négatifs un pouvoir comparable et élevé (de 88% à 95%). Les pourcentages de présence d'allergie aux chiens (15,1%) et aux chats (22,5%) déjà observés dans notre clientèle augmentent à entre 46% et 67% dans le cas d'un résultat positif et s'abaissent à entre 4% et 8% devant un résultat négatif. On peut donc considérer que la principale fonction des cuti-réactions et du RAST est d'exclure le diagnostic d'allergie se manifestant cliniquement.

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The definitive diagnosis of atopic respiratory and conjunctival disease depends on the detection of allergen-specific IgE antibodies. While skin tests, the radioallergosorbent test (RAST), provocation challenge tests, leukocyte histamine release and the Prausnitz–Küstner test have all been used to diagnose allergy, only skin tests and RASTs are widely used for routine clinical diagnosis.

To compare the predictive values of skin tests and RASTs in children with a history of allergy to dogs or cats, we performed both types of test on a sample of patients who attended our outpatient allergy clinic. We chose potential allergy to dogs or cats as the entry criterion for our study since, in addition to being very common in the pediatric

population, these allergies cause easily recognizable respiratory and ocular symptoms in susceptible individuals.

Methods

The study population consisted of 168 children (97 boys and 71 girls) between 1 and 17 (mean 8.5) years of age who were referred to our clinic for investigation of possible clinical allergy to dogs (in 160) or cats (in 168). Clinical allergy was defined as a history of the onset of upper or lower respiratory tract or ocular symptoms after exposure to the animals. The history was elicited by a trained interviewer using standardized questions[1] that included the following.

- Had the child experienced any nasal obstruction, rhinorrhea, sneezing, nasal itching, wheezing or asthma?
- Had he or she complained of itchy, red and swollen conjunctiva when in contact with dogs or cats?
- Did the family own a dog or cat at the time of the interview?

The presence or absence of clinical allergy was confirmed by one of the authors before any diagnostic tests were done.

Skin prick tests, with commercially prepared extracts of dog and cat fur (Hollister-Stier Laboratories, Rexdale, Ont.), were then conducted according to the standard protocol of the Allergy Section of the Canadian Paediatric Society.[2] Negative (diluent) and positive (histamine) controls were used. For a test result to be positive the mean diameter of induration had to be at least 2 mm greater than with the negative control. Serum samples were obtained at the time of testing and stored at −20°C.

RASTs were performed by a modified Pharmacia method. Allergen-conjugated cellulose discs were prepared from the same allergen extracts as used in the skin tests, and the results were expressed as the percentage bound of total radioactivity. A test result was deemed positive if the binding was greater than the mean background binding plus two standard deviations. A standard control curve was obtained for each run with the same allergen-specific pooled reference serum. The maximum dilution used (1:100) invariably gave binding (E value) greater than the upper limit of background binding, and all positive test results were greater than the E value. The specificity of the assay was shown by the inhibition of binding after incubation of the reference serum with soluble allergen.

The skin prick tests and RASTs were performed by technicians blinded to the child's allergy history.

The frequency of negative test results in those with positive and negative histories of clinical allergy to dogs or cats was analysed to elicit the sensitivity, specificity and predictive value of the tests (singly and together) and the post-test probability of disease. The level of RAST binding was compared in those with and without clinical allergy by the Mann-Whitney rank sum test and the Student *t*-test, and the frequency of dog and cat ownership was compared by the chi-square test.

Results

Symptoms were provoked by exposure to dogs in 31 (19%) of 160 children and to cats in 51 (30%) of 168. The sensitivity and specificity of the skin prick tests and RASTs were similar, and combining the tests did not significantly increase the sensitivity (Table I). The positive predictive values were comparable for the skin prick tests and RASTs, ranging from 53% to 76%; the negative predictive values were much higher, 88% to 95%.

Since the predictive value of either test depended on the prevalence rates of clinical allergy to dogs and cats in our study population (which may have been different from those in our larger referral population), we also related the post-test probability of clinical allergy for both positive and negative test results to the frequency with which symptoms provoked by dogs or cats were reported in 1238 consecutive pediatric referrals to our clinic in 1981–1982: 15.1% and 22.5% respectively.[1] The post-test probability of clinical allergy with a positive test result ranged from 46% (skin prick test, RAST or both for dogs) to 67% (RAST for cats), whereas the post-test probability with a negative test result ranged from 4% (skin prick test, RAST or both for cats) to 8% (skin prick test, RAST or both for dogs) (Table I).

To assess whether allergen-specific IgE antibody responses in RAST-positive patients differed according to whether such patients had positive or negative histories of allergic symptoms after exposure to dogs or cats, we compared levels of radioactivity binding in the two groups (Fig. 1). The mean values as a percentage of total radioactivity were higher in the subgroups with a positive history, but the differences were not statistically significant.

Since ownership of a dog or cat could negatively bias the reporting of symptoms, we compared the frequency of pet ownership in the RAST-positive patients with and without positive histories. Of those with dogs 7 of 13 (54%) reported symptoms, and of those without dogs 15 of 24 (62%) reported symptoms. Of those with cats 9 of 11 (82%) reported symptoms, and of those without cats 30 of 42 (71%) reported symptoms. Neither chi-square value was significant. We therefore concluded that there was no evidence of underreporting of symptoms by animal owners.

Discussion

Provocation testing by direct exposure to aller-

gens is useful for determining allergic responsiveness but is technically difficult and subject to many variables.[3-7] Positive results therefore cannot be taken as unequivocally indicative of clinically relevant allergic disease. Clinically the primary consideration is whether a natural exposure to allergen might cause symptoms. Thus, we chose the carefully documented onset of symptoms as our indicator of clinical allergy. It is important to point out that in this study a diagnosis was made before skin prick tests and RASTs were done. This is not necessarily the case in clinical practice, where a less meticulous and detailed history may be possible, and a diagnosis of allergy is often based on the presence of a positive test result.

The results of our study indicate that skin prick tests and RASTs, performed by the methods we have described, are equally effective in diagnosing clinical allergy to dogs and cats. In our referral population, which included nonatopic subjects and is therefore more representative of the general pediatric population than our study sample, only one-half to two-thirds of those with positive results of skin prick tests, RASTs or both are likely to have allergic symptoms. Care must therefore be taken to avoid making a diagnosis of clinical allergy primarily on the basis of a positive test result. In contrast, both types of test are highly efficient in excluding clinical allergy, as was the case in over 92% of our study sample with negative test results. Although it is possible that symptoms may have been denied in some of those with positive test results, we believe this to be unlikely since the frequency of animal ownership was the same in those with positive RAST results, irrespective of whether or not the patients reported symptoms.

Since skin prick tests and RASTs do not appear to differ in their ability to rule in or eliminate the diagnosis of clinical allergy to dogs or cats, the test that is more cost effective, is easier to perform and gives the more rapid result is preferable. Thus, the skin prick test, when carefully performed with a sufficiently potent allergen extract and with adequate positive and negative controls, appears preferable to the RAST for routine use. However, skin testing may be unreliable or unsafe under certain circumstances: when the child has dermatographism, generalized skin disease, atopic eczema plus symptoms suggestive of allergy but negative skin test results, or a history of anaphylaxis (RASTs avoid the risk of a clinical reaction); and when the patient is a young infant with negative skin test results but the cutaneous allergic inflammatory response is suspected of being less well developed than it would be in an adult.[8,9]

Since the presence of allergen-specific IgE antibody merely indicates sensitization to a specific allergen, the lack of significant differences in RAST binding levels between those with and without

Table I — Predictive value of skin prick tests and radioallergosorbent tests (RASTs) and post-test probability of clinical allergy to dogs and cats among 168* children

Test and result	History: Positive	History: Negative	Predictive value (%)	Post-test probability† (%)
Dogs				
Skin prick test				
Positive	21	18	54	47
Negative	10	111	92	7
	Sensitivity 68%			
	Specificity 86%			
RAST				
Positive	22	15	59	52
Negative	9	114	93	7
	Sensitivity 71%			
	Specificity 88%			
Both tests				
Positive	26	23	53	46
Negative	5	106	95	4
	Sensitivity 84%			
	Specificity 82%			
Cats				
Skin prick test				
Positive	39	20	66	57
Negative	12	97	89	8
	Sensitivity 76%			
	Specificity 83%			
RAST				
Positive	39	12	76	67
Negative	14	103	88	8
	Sensitivity 74%			
	Specificity 90%			
Both tests				
Positive	43	23	65	55
Negative	8	94	92	5
	Sensitivity 84%			
	Specificity 80%			

*Only 160 were suspected of being allergic to dogs.
†Prevalence of clinical allergy in referral population: to dogs, 15.1%; to cats, 22.5%.

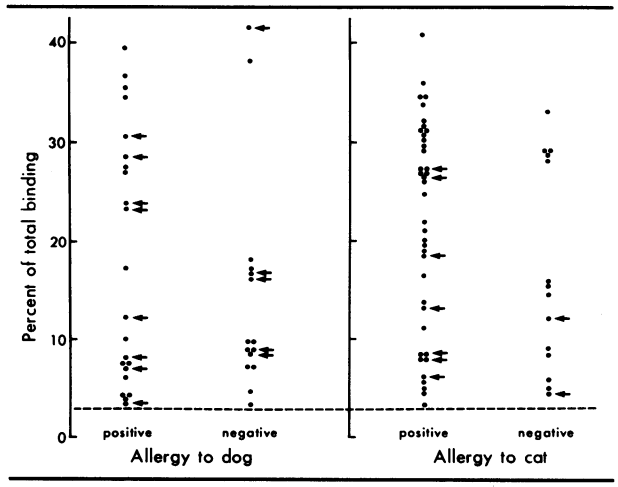

Fig. 1 — Levels of serum IgE allergen-specific antibody (percent of total radioactivity binding) in children with positive results of radioallergosorbent tests. Background radioactivity, mean + two standard deviations, shown by dotted line. Arrows indicate dog or cat ownership.

clinical allergy is not unexpected. The presence of such antibodies is only one of several variables that may influence the development of clinical allergy. Other factors include the quantity of allergen to which the subject is exposed, the duration of exposure, environmental conditions (temperature, humidity and air flow), individual variation in the releasability of mast cell, basophil or macrophage inflammatory mediators, the sensitivity of target organ tissues to the mediators, temporal fluctuations in circulating levels of sympathetic amines and cortisol, and person-to-person variation in endocrine and pharmacologic cellular receptors that modulate allergic tissue responses.

The results of our study must be considered in the context of the allergens used and the methods employed for the skin tests and RASTs. It is possible that studies of other allergens may give different results because of differences in the level of discrimination of positive and negative test results, variations in immunogenicity and the presence of nonspecific inflammatory substances in the allergen extracts.[3,10]

The predictive value and post-test probability of clinical allergy for skin prick tests and RASTs were found to be comparable in diagnosing clinical allergy to dogs and cats. Whereas over 92% of the negative test results were associated with no clinical allergy, only one-half to two-thirds of positive results were associated with symptoms, which emphasizes the importance of the medical history in making a diagnosis of clinical allergy.

We hope that our findings can be applied in clinical practice. For example, if the parents of an allergic child wish to know whether to remove a dog or cat from their home, a negative result of a skin prick test or RAST, by indicating with a high degree of accuracy that the child does not have clinical allergy to the animal, could determine that the pet remains. A positive result, on the other hand, indicates immunologic sensitization but not necessarily clinical allergy. Since skin prick tests and RASTs are equally effective screening tests, skin tests remain the best choice for routine use since they are simpler, give results faster and are more cost effective. RASTs are an efficient alternative when skin tests are contraindicated because of skin disease or diminished skin reactivity.

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