

Efficacy and specificity of immunotherapy with laboratory animal allergen extracts

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The clinical and immunologic response to immunotherapy with laboratory animal allergens was evaluated. There were 23 patients; 11 had received immunotherapy with 12 different extracts (five mouse, six rat, one rabbit), and 12 were matched untreated patients. As a group, nine of 23 had seasonal hay fever. Among the treated patients nine of 11 subjectively improved with immunotherapy. Blocking antibody titers were determined by serum inhibition of allergen-induced histamine release. Treated patients had mean blocking antibody levels of $G_{30} = 59.3 \pm 38.7$. In the untreated patients the antibody level was low ($G_{30} = 4.6 \pm 3.6$). The difference between the two groups was highly significant (t test $p < 0.001$). The blocking antibody level correlates with both the final weekly allergen dose and also the cumulative allergen dose received during immunotherapy. When pretreatment sera were available a temporal rise in blocking antibody was demonstrated during immunotherapy. In patients allergic to several laboratory animals and treated with one allergen, the blocking antibody response was predominantly specific to the allergen used in immunotherapy. This indicates a lack of cross-reactivity in the IgG response to the major animal allergens. When immunotherapy was discontinued in four patients there was a dramatic decrease in the blocking titer, and after 24 mo the levels were the same as those of untreated patients.

Allergic reactions to animals are an important occupational health problem among individuals who work with laboratory animals.¹⁻³ Such patients are usually instructed to avoid contact with the offending animals. However, in some cases of occupational allergy to laboratory animals complete elimination of exposure to allergen is not possible and symptomatic treatment not sufficient. In such cases immunotherapy has occasionally been attempted.⁴⁻⁵ However, there is no information on the immunologic response to hyposensitization therapy with laboratory animal allergens.

A number of studies have demonstrated the effectiveness of immunotherapy with pollen allergens⁶⁻⁸

and in cat-sensitive allergic individuals.⁹ Hyposensitization results in a decrease in clinical symptoms, accompanied by the development of specific blocking antibodies of the IgG class in the serum^{7, 8, 10} and of the IgA class in nasal secretions.¹¹ The level of specific IgE antibodies in the serum is frequently reduced during immunotherapy.¹² Blocking antibodies have been measured by several methods including inhibition of allergen-induced leukocyte histamine release,¹³ passive hemagglutination,¹⁴ radioallergosorbent assay utilizing an anti-IgG serum¹⁵ or protein A,¹⁶ enzyme-linked immunoassay,¹⁷ binding of radio-labeled antigen,¹⁸ and double-antibody radioimmunoassay for antigen-specific IgG.¹⁸ In our study blocking antibody titers were determined by inhibition of histamine release with allergen preincubated with serum. This blocking assay does not require purified allergen and is not influenced by the ability to label or couple the relevant allergens to solid supports.

This study was initiated to evaluate the blocking antibody response to hyposensitization with animal allergens. Serum of treated patients had significant levels of blocking antibody; the level of these antibodies correlated with the total allergen dose the

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TABLE I. Clinical data on animal-allergic patients

Patient	Age/sex	History of Symptoms to					Length of exposure (yr)	Interval between exposure and onset of symptoms (yr)	Seasonal hay fever	IgE (ng/ml)
		Mou	Rab	Rat	G.P.	H.				
Treated										
J. C.	34/M			+			8	2	—	154
R. G.	30/M	+		+	+	+	5	2	—	1,724
P. G.	31/M			+			12	8	+	24
S. B.	34/F		+		+		14	13	—	901
C. F.	41/F	+		+			8	2	+	706
B. H.	33/F	+		+			12	3	—	110
S. R.	31/M	+	+	+	+	+	9	<1	—	765
M. M.	29/F	+		+			8	<1	—	60
L. S.	26/F			+	+		3	1	—	523
R. M.	26/M			+			5	1	—	72
J. R.	30/M	+	+	+	+		5	<1	+	328
							$\bar{x} = 8.1$	$\bar{x} = 2.9$	3/11	$\bar{x} = 488$
							$S_x = 1.1$	$S_x = 1.1$		$S_x = 156$
Untreated										
W. H.	46/M	+	+	+	+	+	24	<1	+	1,491
L. W.	31/M	?	?	?	?	?	10	6	—	221
A. B.	37/M		+				10	7	+	854
T. S.	39/M	+			+		6	3	—	595
D. S.	35/M	+	+		+		9	<1	—	45
L. D.	37/M			+			16	<1	+	284
J. H.	26/M	?	?	+	?	?	6	<1	+	130
J. D.	31/M	+		+			10	6	—	284
C. L.	41/F	+	+	+	+	+	13	<1	+	1,857
C. F.	39/F	+		+			6	2	+	266
M. M.	28/F	+		+			7	<1	—	ND
J. C.	32/M			+			6	2	—	121
							$\bar{x} = 10.3$	$\bar{x} = 2.4$	6/12	$\bar{x} = 559$
							$S_x = 1.6$	$S_x = 0.7$		$S_x = 182$

Mou = mouse; Rab = rabbit; G.P. = guinea pig; H = hamster; ND = not done; HR = histamine release score.

Histamine-release tests performed with whole blood. Range of possible scores 0 to 10. Score of less than 1 indicates histamine release was negative. Scores between 1 and 10 proportional to both the cell sensitivity and reactivity.

*Intradermal skin test with 100 PNU/ml. A dash (—) indicates negative skin test.

patients had received. The blocking antibody was specific for the allergen injected. The effect of discontinuing treatment on the blocking antibody was also studied.

MATERIALS AND METHODS

Solutions

A Pipes-buffered (pH 7.4) medium was used containing NaCl 110 mM, KCl 5 mM, NaOH 40 mM, Pipes 25 mM, and 0.03% HSA (Pipes A). To this medium 2 mM Ca^{++} and 0.5 mM Mg^{++} were added to prepare Pipes ACM used for diluting serum, antigen, and cells for the histamine release reaction. Stock edetate (EDTA) solution was 0.1 M at pH 7.2.

Materials

Allergen extracts used in this study were obtained from Hollister-Stier Laboratories. The animal allergens are an extract prepared from the whole pelt of animals and were in 50% glycerin. Mixed ragweed contained equal amounts of giant and short ragweed pollen; mixed grasses contained equal amounts of timothy, rye, orchard, Kentucky blue, fescue, redtop, and sweet vernal pollen. Mixed trees consisted of equal parts of ash, beech, birch, elm, hickory, oak, and poplar pollen. Mixed molds contained equal parts of *Alternaria*, *Hormodendrum*, *Helminthosporium*, *Aspergillus*, and *Penicillium*. For the histamine-release experiments the allergens were used after dialysis against phosphate-buffered saline.

A serum pool was prepared from a nonallergic donor

Ragweed		Grass		Trees		Molds		Dust		Mouse		Rabbit		Rat		Guinea pig		Hamster	
Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR	Skin test*	HR
Treated																			
-	0	-	0	-	0	-	0	1+	1	2+	3	1+	0	4+	9	2+	1	2+	1
-	0	-	0	-	0	-	0	2+	1	4+	8	2+	1	3+	8	4+	9	4+	9
3+	4	-	0	-	0	1+	1	-	0	-	6	-	0	3+	5	-	0	-	0
-	ND	3+	ND	-	ND	-	ND	2+	ND	1+	ND	2+	4	1+	ND	1+	ND	1+	ND
2+	5	-	0	-	3	-	0	1+	8	3+	9	2+	9	3+	9	-	5	-	9
-	0	-	0	-	0	-	0	-	0	-	0	-	0	4+	2	-	0	-	0
-	1	-	0	-	0	-	0	3+	4	4+	9	2+	8	2+	8	4+	8	-	ND
-	0	-	0	-	0	-	0	2+	0	3+	1	2+	0	3+	1	2+	0	3+	0
-	0	-	0	-	0	-	0	-	0	-	0	3+	2	3+	2	3+	2	-	0
-	0	-	0	-	0	-	0	-	0	-	1	-	0	3+	2	-	0	-	0
4+	9	-	0	-	0	-	0	-	0	1+	1	-	0	4+	3	4+	5	-	0
Untreated																			
3+	7	4+	9	4+	6	-	2	2+	3	2+	8	3+	8	3+	7	4+	1	2+	1
-	0	-	0	-	0	-	0	-	1	4+	7	4+	8	4+	9	4+	8	4+	7
4+	10	-	0	4+	6	-	0	3+	2	3+	8	-	0	4+	8	2+	0	3+	3
2+	5	3+	8	3+	8	-	0	2+	5	4+	10	3+	10	4+	10	4+	10	4+	10
-	0	-	0	-	0	-	0	2+	1	3+	6	3+	0	3+	4	4+	5	4+	7
-	2	4+	10	2+	0	-	2	2+	1	2+	1	-	0	3+	8	-	1	2+	5
2+	0	4+	10	2+	0	-	0	2+	2	-	0	2+	0	2+	8	1+	0	1+	0
2+	0	-	0	-	0	-	0	-	4	4+	8	2+	4	4+	10	2+	1	2+	4
4+	10	2+	1	3+	9	-	0	1+	3	4+	10	4+	10	4+	10	4+	10	3+	7
2+	5	-	0	-	3	-	0	1+	8	3+	9	2+	9	3+	9	-	5	-	9
-	0	-	0	-	0	-	0	2+	0	3+	1	2+	0	3+	1	2+	0	3+	0
-	0	-	0	-	0	-	0	1+	1	1+	3	1+	0	4+	9	2+	1	2+	1

with blood type AB positive (normal human serum [NHS]) and kept frozen in small aliquots at -20°C .

Clinical evaluation

The patients in this study were seen in the Employee Allergy Clinic at the National Institutes of Health. The patients were evaluated by history and intradermal skin tests. For skin tests 0.02 ml allergen was injected at each site on the upper arm with a disposable syringe and the reactions read at 15 min. Skin-test grading was based on measurements of the wheal with the use of the following criteria: negative, site no different from a diluent control; 1+, <5-mm wheal; 2+, 5- to 10-mm wheal; 3+, 10- to 15-mm wheal without pseudopods; 4+, >15-mm wheal with or without pseudopods or >10-mm wheal with pseudopods. The highest concentration used for skin tests was 100 protein nitrogen units (PNU)/ml, and where appropriate

the skin tests were initiated with lower allergen concentrations.

Immunotherapy

Allergens obtained commercially were utilized for immunotherapy. Injections were on a weekly basis. The allergen dose was started at 5 PNU and increased gradually depending on the patient's sensitivity. Among these treated patients there were no systemic reactions, and immunotherapy was not discontinued in any patients because of reactions. The maximum weekly dose ranged from 2,000 to 10,000 PNU.

Histamine release from whole blood

Histamine release from whole blood with a panel of allergens was performed at the time of the first clinic visit to evaluate the reactivity of these patients. The method has

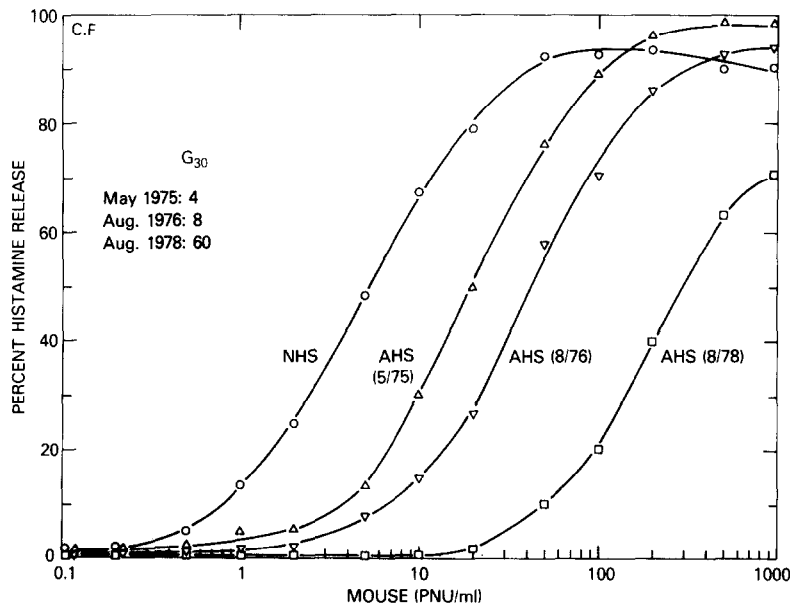


FIG. 1. Serial changes in blocking antibody levels. This mouse-allergic patient had received immunotherapy since May 1975. Normal human serum (NHS) and patient serum samples (AHS) from May 1975, August 1976, and August 1978 were incubated with mouse allergen extract and then added to the patient's cells. The shift of the curves demonstrates the increase of blocking antibodies expressed as the G_{30} AHS/NHS.

been described previously.²⁰ Briefly, 25 ml venous blood was drawn into a plastic syringe and transferred to a plastic tube (50 ml, Falcon No. 2070) containing 0.5 ml heparin (Liquemin sodium 10, sodium heparin injectable, 1 ml = 1,000 U, Organon, West Orange, N. J.). The blood was kept at 4° C and tested within 4 to 6 hr. Just prior to use in the test the blood was diluted with ~5 ml Pipes ACM and used directly in the histamine-release reaction. The allergens were diluted in Pipes ACM and tested at concentrations of 1, 10, and 100 PNU/ml. Histamine release reactions were carried out in 12 × 75 mm plastic tubes; 0.5 ml Pipes ACM or allergen was added to the tubes in the ice bath, 0.5 ml diluted blood was then added to all the tubes, and racks were transferred to a 37° C bath. The racks were shaken every 10 min. In each experiment perchloric acid at a final concentration of 6% was added to some samples to obtain the total histamine content of blood. After 60 min the tubes were transferred to an ice bath and centrifuged at 2,500 rpm (1,200 × g) for 30 min at 4° C. The supernatants were decanted and assayed for histamine.

The scoring system previously described was used to summarize the histamine release data.²¹ The range of possible scores is 0 to 10; a score less than 1 indicates that the histamine release was essentially negative, with little or no histamine release at any allergen concentration. Scores between 1 and 10 are proportional to both the cell sensitivity and reactivity; highest scores are from tests when histamine release occurred at all three allergen concentrations.

Preparation of washed leukocytes

Blood from patients was collected in plastic syringes and anticoagulated with 0.01 M EDTA. It was sedimented at room temperature for 60 to 75 min with 2.5 ml dextran

(clinical dextran 6% in 0.85% NaCl to which 3% glucose was added) per 10 ml blood. The upper layer containing leukocytes, platelets, and plasma was transferred to another plastic tube and centrifuged at 300 × g for 8 min at 4° C. The pelleted cells were suspended in Pipes A containing 4 mM EDTA centrifuged at 300 × g for 8 min at 4° C. The cells were then washed in Pipes A. After centrifugation the cells were suspended in Pipes ACM buffer.

Blocking antibody titration

Leukocytes were isolated from those patients allergic to laboratory animals. Blood samples from the treated group were taken 5 to 6 days after the last allergen injection. Serum from these patients was obtained on the day of the experiment; pretreatment sera had been kept frozen at -20° C. A 0.1-ml aliquot of either the patient's serum (allergic human serum [AHS]) or NHS at a concentration of 30% was mixed with 0.1 ml antigen at concentrations previously determined to be appropriate for the patient's histamine-release curve. After incubation of the antigen and serum for 60 min at 37° C 0.1 ml prewarmed leukocytes were added to each tube. The final serum dilution was therefore 10%. The mixture was incubated at 37° C for 40 min and the reaction then stopped by adding 0.2 ml cold Pipes A containing 4 mM EDTA. After mixing the tubes were centrifuged and the supernatants assayed for histamine. Titrations utilized three different concentrations per 10-fold increase in antigen levels. In all experiments reaction tubes were in duplicate. Blanks contained cells, buffer, and serum; the histamine release in these tubes did not exceed 10% of the completes. Cellular histamine content for each experiment was determined by perchloric acid lysis of cells.

In all these experiments blocking antibody determina-

tions were performed utilizing cells and serum from the same patient.

The level of the blocking antibodies are expressed as:

$$G_{30} \frac{\text{AHS}}{\text{NHS}} = \frac{\text{AHS-HR}_{30}}{\text{NHS-HR}_{30}}$$

where AHS-HR₃₀ refers to the concentration of allergen required for 30% histamine release in the presence of AHS, and NHS-HR₃₀ is the concentration of allergen required for 30% histamine release in the presence of NHS. As pointed out by Lichtenstein and Osler,¹³ this technique actually measures the percentage of added antigen bound by 10% allergic serum.

Total serum IgE

Determination of total serum IgE was kindly performed by Dr. T. Waldmann, National Institutes of Health. The values are expressed as nanograms per milliliter.

Histamine assay

Histamine was assayed by an automated fluorometric technique.^{22, 23} Calculations were as described previously.

Statistical methods

The mean, standard deviation, standard error, t statistic for two means, and Spearman's rank correlations were calculated using a Hewlett-Packard 65 calculator.

RESULTS

Selection of patients

The patients in this study had developed allergic symptoms on exposure to laboratory animals. Allergy to animals was confirmed by history, intracutaneous skin test, and leukocyte histamine release. Most of the patients had symptoms on exposure to several different species of laboratory animals.

Clinical information on all the patients is shown in Table I. Eleven patients had received immunotherapy with 12 different extracts (five mouse, six rat, one rabbit). All experienced hay fever-type symptoms on exposure to laboratory animals, and eight also developed asthma. The mean length of exposure to laboratory animals was 8.1 yr, with first allergy symptoms being noticed after an average interval of 2.9 yr. Three of the 11 patients had a history of seasonal hay fever, and five of the 11 had serum IgE levels above 500 ng/ml.

A group of matched untreated patients was selected for study (Table I). The length of exposure to laboratory animals in these patients was 10.3 yr, with 2.4 yr between initial exposure and onset of allergy symptoms. These values were not significantly different from those for the treated patients. Eight of 12 patients had asthmatic symptoms on exposure to animals; four of these 12 had serum IgE levels above 500 ng/ml, and six had seasonal hay fever. In general the levels of skin reactivity were higher in the control

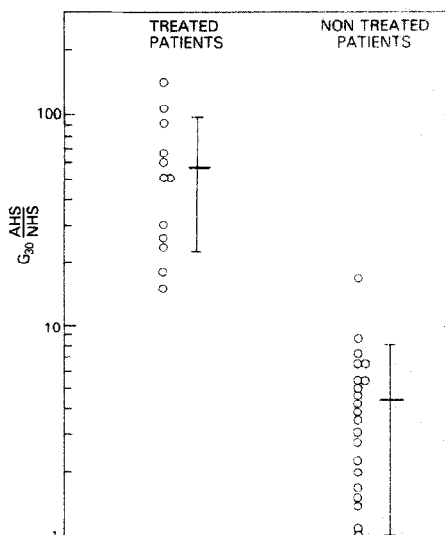


FIG. 2. Blocking-antibody levels to allergens of laboratory animals. Treated patients had received immunotherapy for at least 12 mo. The blocking-antibody titer is expressed as G_{30} AHS/NHS. Treated patients: $\bar{x} = 59.3$, $SD = 38.7$. Untreated controls: $\bar{x} = 4.6$, $SD = 3.6$. The difference between the two groups is significant by a t test at $p < 0.001$.

than in the treated groups. However, the histamine release scores of the treated and untreated patients were not significantly different.

Among the patients who received immunotherapy, nine of 11 reported a decrease in symptoms. No further attempts were made to quantitate their symptoms, because of the variable exposure of these patients to laboratory animals.

Blocking antibody response

The serial changes in blocking antibody levels of a patient treated with mouse allergen is shown in Fig. 1. There was minimal increase in blocking antibody level during the first year of immunotherapy (the initial G_{30} of 4 rose to 8). However, during the next 2 yr of therapy the blocking titer rose to 60.

The blocking antibody levels of treated and untreated patients were compared (Fig. 2). Patients who had not received immunotherapy have low levels of blocking antibody ($\bar{x} = 4.6$, $SD = 3.61$). These levels are similar to those of untreated pollen-allergic patients.^{13, 24} The patients treated with laboratory animal allergen had much higher blocking antibody levels ($\bar{x} = 59.3$, $SD = 38.7$). The difference in blocking antibody levels between the treated and untreated groups is highly significant ($p < 0.001$). The blocking antibody level correlates well with both the final allergen maintenance dose ($r = 0.66$, $p < 0.05$) and the cumulative allergen dose given during immunotherapy ($r = 0.70$, $p < 0.02$) (Fig. 3). However,

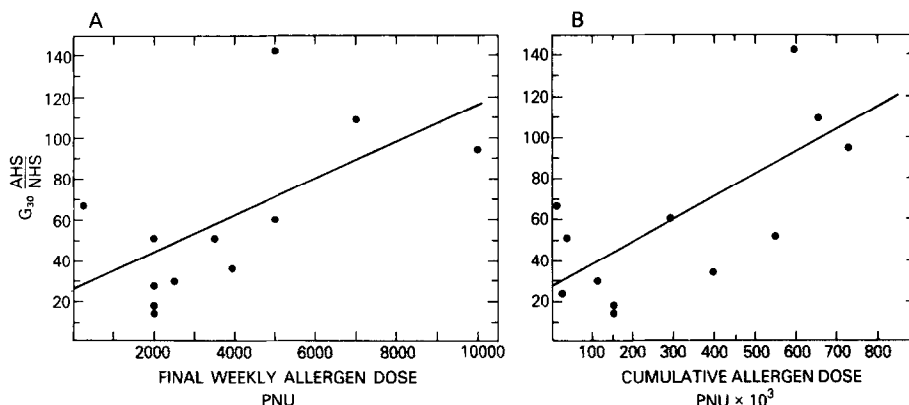


FIG. 3. Correlation between the level of blocking antibody and the allergen dose received during immunotherapy. *A*, Correlation to the final weekly allergen dose $r = 0.63$, $p < 0.05$ ($y = 25.8 + 0.01x$). *B*, Correlation to the cumulative allergen dose $r = 0.70$, $p < 0.02$ ($y = 24.0 + 0.00011x$).

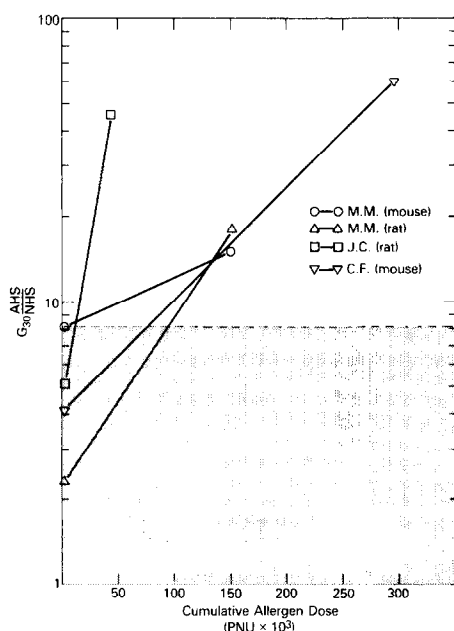


FIG. 4. Increase in blocking-antibody levels following immunotherapy. The levels of blocking antibodies before and after immunotherapy are shown for three patients, one of whom had been treated with both rat and mouse extract. Gray zone, the blocking titer of untreated animal-sensitive patients ($\bar{x} \pm SD$).

there was no correlation between blocking antibody and the duration of immunotherapy (data not shown).

There is wide variation in the response of individual patients to immunotherapy. This variation is clear from the response of patients who had received the same cumulative dose of allergen (Fig. 3, *B*). Pretreatment sera were available from three patients who had been treated with four allergens (Fig. 4). The blocking antibody levels prior to treatment were in the same range as those of untreated patients (Fig. 2).

After immunotherapy there was a significant increase in the level of the blocking antibody. Whereas patient J. C. had a marked blocking antibody response after treatment with only 50,000 PNU, patient M. M. responded poorly after being treated with a dose of rat and mouse allergens three times higher. Patient CF responded poorly during the first year of treatment with mouse allergen but showed increased levels of blocking antibodies during the following 2 yr (Fig. 1).

Specificity of blocking antibody response

There is little information on the cross-reactivity between different animal allergens. Therefore we tested the antigen specificity of the blocking antibody response in individuals who were allergic to several laboratory animals and had been treated with only one allergen. The results of the treatment of a patient allergic to mice, rats, rabbits, and guinea pigs with mouse allergen is shown in Fig. 5. Treatment with mouse allergen resulted in blocking antibodies that were highly specific for mouse antigens; the blocking levels to rat, rabbit, and guinea pig were within the range of untreated patients. A summary of all the specificity data is shown in Fig. 6. Three patients allergic to both rats and mice and treated with rat allergens had rat-specific blocking antibodies with no response to mouse allergens (Fig. 6, *A*); there was also no response to hamster allergen in the one patient who was also allergic to hamsters. Three patients were treated with mouse allergens, and all three developed blocking antibodies to mouse antigens (Fig. 6, *B*). All three were also allergic to rats but had no blocking antibodies to rat allergens. There were also no cross-reactivities with guinea pig or rabbit allergens. However, in one patient treated with mouse allergen there was blocking antibody activity against hamster allergens.

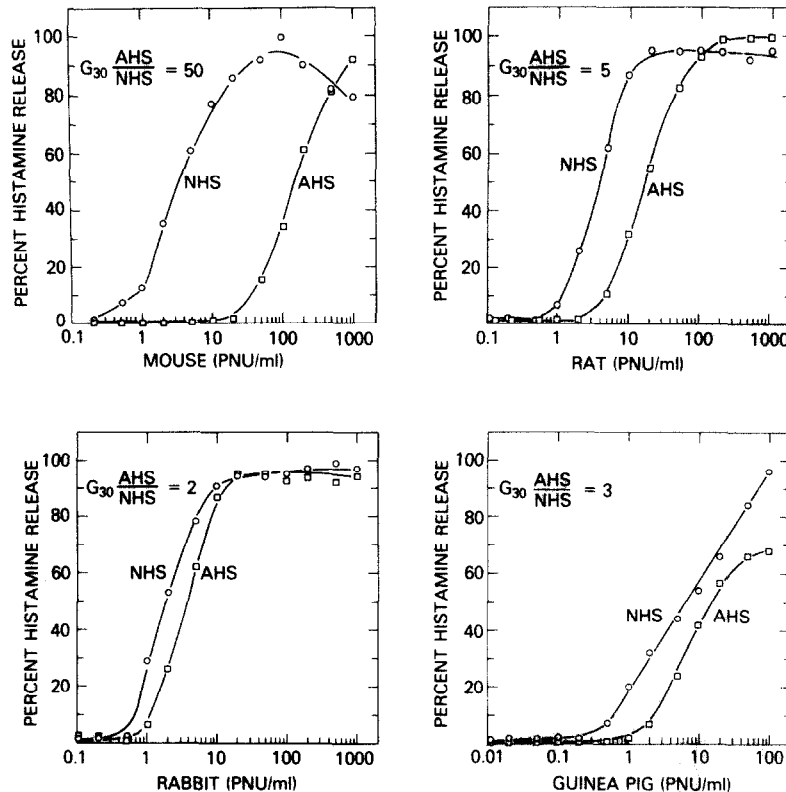


FIG. 5. Specificity of blocking-antibody response to immunotherapy with mouse skin extract. A patient allergic to mice, rats, rabbits, and guinea pigs was treated with mouse skin extract (total dose 550,000 PNU).

Blocking antibody levels following termination of immunotherapy

The effect of discontinuing immunotherapy on the blocking antibody level was studied. Therapy was terminated in four patients who stopped working with laboratory animals. These patients had been receiving therapy for 15 to 24 mo. The level of blocking antibody decreased when they were tested 16 to 36 mo after immunotherapy was stopped (Fig. 7), and in three of these patients the levels were within the range of untreated patients.

DISCUSSION

This study demonstrates the effectiveness of immunotherapy with laboratory animal allergens in causing an increase in blocking antibodies. The blocking antibody levels in the treated patients were about 12 times higher than in the control group. The antibody level correlates with the cumulative allergen injected and also with the final weekly maintenance allergen dose. Our data do not indicate that the final weekly allergen dose is more important in inducing a higher blocking antibody titer. Similar levels of blocking antibody have been found in pollen-allergic patients treated with pollen allergens.²⁴

In studies demonstrating the effectiveness of immunotherapy a parallel rise in blocking antibody titer has been observed.^{6-8, 12, 18, 19} There is also some correlation between the blocking antibody response and clinical improvement.⁷ In some studies symptomatic improvement has been correlated to the allergen-specific IgG-IgE ratio.²⁵ Immunotherapy with cat allergen caused a reduction in skin reactivity and bronchial sensitivity to cat pelt extract after treatment.⁹

A characteristic of individuals allergic to laboratory animals is that they are reactive to a number of different animals. For example, among the patients in this study about 78% had skin reactivity to both mice and rats; 65% reacted to mice, rats, and guinea pigs. On the basis of such observations it has been suggested that different mammals share similar or identical allergens.²⁶ However, the blocking antibody response of these patients appears to be specific (Fig. 6). Six patients were allergic to both rats and mice; three were treated with mouse and three others with rat extracts. The blocking antibody in all six patients discriminates between rat and mouse allergen extracts. The only case of a nonspecific blocking antibody response was in a patient who was treated with

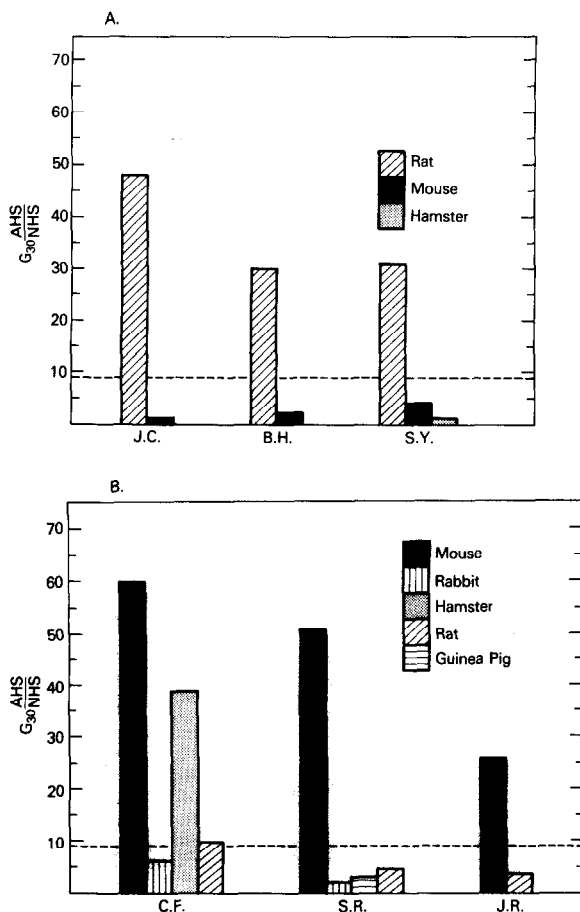


FIG. 6. Specificity of blocking-antibody response to treatment with animal skin allergens. *A*, Patients treated with rat allergens. *B*, Patients treated with mouse allergens. *Dashed line*, upper limit of the blocking titer of untreated animal-sensitive patients ($\bar{x} \pm SD$).

mouse allergens and developed blocking antibodies to both mice and hamsters. This would suggest cross-reactivity between hamster and mouse allergens.

Among these animal-allergic individuals only 39% (nine of 23) had seasonal hay fever. This is a higher percentage than the fraction of the general population with pollen allergy. However, as everyone is exposed to pollens, the lack of seasonal hay fever in a fraction of these animal-allergic patients is very significant. Therefore, although pollen-allergic individuals are at higher risk of developing allergy to laboratory animals, non-pollen-allergic individuals are also at risk.

In this group of treated patients nine of 11 felt symptomatically improved. No objective criteria were used to further corroborate this observation. The exposure to laboratory animals is erratic and is not comparable among different individuals; e.g., exposure is frequently to animals in the hall or to animal rooms adjacent to the laboratory where these patients work, or the patient might be exposed to another scientist

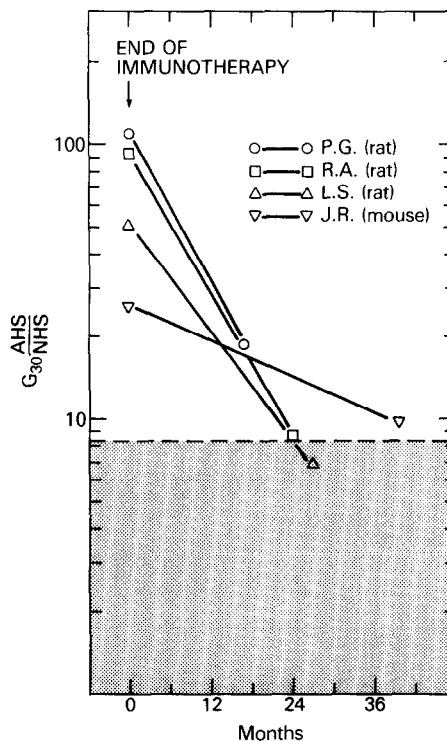


FIG. 7. Decrease of blocking-antibody titer in patients who had discontinued immunotherapy. *Gray zone*, blocking-antibody titer of untreated animal-sensitive patients ($\bar{x} \pm SD$).

who is carrying allergens on his or her clothes. This type of variation makes symptom diaries useless and the variation among different patients who work at different locations (e.g., buildings, floors) immense.

Blocking antibody determination was performed using each individual's own leukocytes for the histamine-release studies. In studies with unpurified multiallergenic extracts it is important to determine that the blocking antibody activity is directed toward antigens and antigenic determinants to which the individual is sensitive.

Of interest, the blocking antibody levels fell when desensitization was discontinued. However, had the patients been treated for a longer time, the blocking titer might have persisted longer.

Although our results indicate clinical and immunologic improvements from immunotherapy with animal allergens, it should be emphasized that avoidance still is the treatment of choice. The wide variation in different allergen batches is well recognized; therefore our findings may not extend to other commercial dander extracts or even to other batches made by the same company. This study demonstrates that immunotherapy does result in the development of specific blocking antibodies. A double-blind controlled trial is therefore indicated to unequivocally test

the efficacy of immunotherapy with laboratory animal allergens.

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