

Canine atopic dermatitis: a retrospective study of 169 cases examined at the University of California, Davis, 1992–1998.

Part II. Response to hyposensitization

GILA ZUR*, STEPHEN D. WHITE†, PETER J. IHRKE‡, PHILIP H. KASS‡ and
NINA TOEBE§

*Koret Veterinary Teaching Hospital, School of Veterinary Medicine, The Hebrew University of Jerusalem,
PO Box 12 Rehovot 76100, Israel

Departments of †Medicine and Epidemiology, and
‡Population Health and Reproduction, and

§Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of California,
Davis, CA 95616, USA

(Received 5 April 2000; accepted 17 July 2001)

Abstract One hundred and sixty-nine dogs were diagnosed with atopic dermatitis, and treated with hyposensitization for at least 1 year based on the results of either intradermal skin tests (IDST) or enzyme-linked immunosorbant serum assays (ELISA). Excellent (i.e. hyposensitization alone controlled clinical signs), good (> 50% improvement), moderate (< 50% improvement) and no (clinical signs were unchanged) responses were seen in 19.5, 32.5, 20.1 and 27.8%, respectively. Age of onset, age when treatment was initiated or the duration of clinical signs had no influence on response to hyposensitization. Dogs having concurrent flea allergy dermatitis were statistically more likely to respond better than dogs with concurrent food allergies. Although not statistically significant, there were trends for Golden Retriever and male dogs to respond better than other breeds and female dogs, respectively. Dogs having more than 21 positive reactions in allergy tests and treated with more than 21 allergens had lower response scores, and a longer time course before achieving beneficial response. Lower response scores were seen in dogs having positive reactions to cultivated plants, grasses, trees or insects. There was no difference in response to hyposensitization whether based on IDST or ELISA results.

Keywords: atopic dermatitis, dog, ELISA, flea, hyposensitization, intradermal skin test.

INTRODUCTION

Canine atopic dermatitis (CAD) is a common skin disease characterized by an inherited tendency to develop IgE antibodies in response to environmental allergens.^{1–7} The pathophysiology appears similar to that seen with human asthma or hay fever. Diagnosis is based on history and clinical presentation and is further substantiated by finding positive reactions to specific allergens using an *in vivo* intradermal skin test (IDST) or *in vitro* serological tests such as enzyme-linked immunosorbant test and radioallergosorbant test (ELISA and RAST, respectively).^{1,3,8–12}

The primary function of these tests is to confirm the clinical diagnosis and select allergens for hyposensitization. Avoidance of the specific allergens is not usually possible, symptomatic therapy with glucocorticoids may cause undesirable side effects and antihistamines are often not successful as the sole treatment; thus hyposensitization is the treatment of choice. Hyposensitization with the offending allergens is the most effective

method of dealing with allergic respiratory disease in humans when symptomatic treatment has failed or cannot be used.^{4,13,14}

There are several hypotheses for the mechanism of action of hyposensitization. The primary theory for the past 40 years has been that injections of small amounts of the specific allergens causes the patient's immune system to develop IgG antibodies (blocking antibodies).¹⁵ These antibodies bind to the specific allergens in the circulation before they are able to combine with IgE on the surface of cutaneous mast cells. This blocking thereby prevents the mast cells from degranulating and releasing histamine and other pruritic mediators. Other theories of the mechanism of hyposensitization include the induction of suppressor T cells, alteration in the balance of T helper (Th)1/Th2 cells, the formation of anti-idiotypic antibodies, alterations in the susceptibility of mediator-secreting cells, reduced levels of circulating IgE, diminished end-organ responsiveness or some combination of the above.^{1,2,8,16–18}

In people receiving hyposensitization, an increase in the serum level of allergen-specific IgG is well correlated with improvement in allergic clinical symptoms.¹⁹ However, there are studies in people that do not show a correlation between immunological and clinical

Correspondence: G. Zur, Koret Veterinary Teaching Hospital, School of Veterinary Medicine, The Hebrew University of Jerusalem, PO Box 12 Rehovot 76100, Israel. E-mail: zurgila@agri.huji.ac.il

Vial 1 (200 PNU mL ⁻¹)		Vial 2 (2000 PNU mL ⁻¹)		Vial 3 (20 000 PNU mL ⁻¹)	
Day	Amount (mL)	Day	Amount (mL)	Day	Amount (mL)
0	0.1	10	0.1	20	0.1
2	0.2	12	0.2	22	0.2
4	0.4	14	0.4	24	0.4
6	0.8	16	0.8	26	0.8
8	1.0	18	1.0	28	1.0*

*1.0 mL from of the same concentration is then given once a week.

Table 1. Protocol for hyposensitization utilized at UCD-VMTH

data.²⁰ Recently, allergen hyposensitization in people has been shown to suppress the release of interleukin (IL)-4 and IL-5, increase the rate of release of interferon-gamma (IFN γ) from T cells, and reduce histamine-releasing activity in peripheral blood mononuclear cells.^{18,21} In dogs, specific hyposensitization resulted in an increase in the serum concentration of allergen-specific IgG.^{17,22}

Although hyposensitization is a well-known method for the treatment of dogs with atopic dermatitis and has been used for that purpose since the late 1960s, standardized regimens have not been established. Veterinary dermatologists and allergists use a variety of allergens, which vary in number, volume, concentration, manufacturer, being aqueous or alum-precipitated, and in various hyposensitization schedules.

The aim of the study was to evaluate the response of atopic dogs to treatment with hyposensitization at the University of California at Davis, Veterinary Medical Teaching Hospital (UCD-VMTH), and to establish if these responses correlated with clinical features and epidemiological parameters.

MATERIALS AND METHODS

Dogs

We retrospectively evaluated 266 medical records of dogs that were examined at the UCD-VMTH during the years 1991–98, diagnosed with CAD according to history, clinical signs and confirmation with positive responses on allergy testing, and that were candidates for hyposensitization. All the dogs had at least two positive results on allergy testing. There were 169 dogs from which a fully detailed response after at least 1 year of treatment was obtained and these were the dogs included in the study.

Allergy testing

Allergy tests were performed as described previously.²³

Concurrent treatments

As in most studies of hyposensitization, almost all the dogs in the study received concurrent treatment with topical and/or systemic medications. For example, all the dogs with otitis externa were maintained on regimens of ear cleansing and medication. Forty-one dogs continued to need ear medication during the study period.

Approximately one-third of the dogs (66) required oral glucocorticoids in order to relieve their pruritus. A

prednisone–trimeprazine combination medication (Temeril-P®, Pfizer Animal Health, Exton, PA, USA) was given to 25 of the 66 dogs. This resulted in very low doses of prednisone being administered (average dose, 2 mg of prednisone and 5 mg of trimeprazine per 10 kg body weight). In 76 dogs, various antihistamines (diphenhydramine, hydroxyzine, clorpheniramine, clemastine) were used adjunctively to control the pruritus during hyposensitization. Fewer than half of the dogs (80) received various omega-3 and omega-6 fatty acid-containing supplements.

Approximately one-third (65 dogs) of the dogs occasionally required antibiotic treatment for concomitant pyoderma. In most cases, a first-generation cephalosporin (cephalexin) was used. Sixteen dogs were treated with oral ketoconazole for coexistent *Malassezia* dermatitis.

Topical treatment, including various antipruritic, antibacterial and anti-yeast shampoos or leave-on conditioners, was utilized in most of the dogs. Sixty dogs received antipruritic topical treatments, 51 dogs received topical antibacterial therapy and 20 dogs received topical treatment for concurrent *Malassezia* dermatitis.

Hyposensitization

The solutions of allergens prepared for hyposensitization included allergens that were positive in the various tests (+3 and +4 in IDST and +2 and above in ELISA tests) if the positive reactions were deemed relevant to that individual based on a history of exposure. Allergens chosen for hyposensitization did not include fleas, insects, sheep's wool and cat epithelia, as they are considered to be controversial as to efficacy in hyposensitization.² Aqueous allergen solutions prepared by the immunology service of the UCD-VMTH were injected subcutaneously by the owners or the referring veterinarian according to the protocol in Table 1. Whenever the total number of selected allergens exceeded 11, the option of dividing the allergens into two separate vials for hyposensitization was offered to the client; however, this was usually declined, as it doubled the expense. When the use of more than one vial was declined we choose the 12–17 allergens most consistent with the exposure history of the dogs.

If diminution of clinical signs was noted in response to the weekly injection of the maintenance solution, an attempt was made to increase the time interval between injections. Any recurrence of pruritus that was not due to concurrent pruritic skin disease led to a recommendation to shorten the interval between injections. These modifications of the protocol were done on an individual basis.

Response to hyposensitization

Response to hyposensitization was scored on a scale of 1–4.

- 1 = No response. The pruritus was unchanged, and no reduction in concurrent antipruritic medications was possible.
- 2 = Moderate response. Less than 50% improvement in pruritus and/or decrease in the number of recurrences of bacterial pyoderma or *Malassezia* dermatitis, with concurrent treatment with antihistamines and/or reduced doses of systemic glucocorticoids.
- 3 = Good response. More than 50% improvement in pruritus and/or decrease in the number of recurrences of bacterial pyoderma or *Malassezia* dermatitis, with concurrent treatment with antihistamines and/or reduced doses of systemic glucocorticoids.
- 4 = Excellent response. More than 50% improvement in pruritus and/or decrease in the number of recurrences of bacterial pyoderma or *Malassezia* dermatitis without concurrent systemic antipruritic treatment, such as glucocorticoids, antihistamines or essential fatty acids.

The degree of response was determined from the clinical records of re-evaluation examinations, from histories taken from the owners, and to a lesser extent, the clinician's impression. The length of time taken to achieve the response was also recorded. For those dogs that had not been evaluated on an on-going basis, a telephone survey was performed. The owners were asked to score the dogs' responses according to the scale above, and to determine the time necessary to achieve that response.

Parameters evaluated

Correlation was investigated between the responses and various parameters. These included breed, sex, age of onset, age at initiation of hyposensitization, duration of clinical signs before hyposensitization was initiated, seasonality of clinical signs, relation to particular seasons, season when hyposensitization was begun, otitis externa, *Malassezia* otitis, distal limb pruritus and/or lesions, *Malassezia* dermatitis, concurrent allergic skin diseases, different allergens, number of allergens used and the response time (duration until beneficial response was achieved).

Statistical methods

Allergens were grouped for statistical analysis: house dust, dust mites, trees and shrubs, grasses, weeds, cultivated plants, moulds and miscellaneous allergens.²³ The statistical analysis was performed multiple times considering both the number of allergens in each group, as well as considering each group as one unit (a 'yes' or 'no' method). Hyposensitization responses were evaluated statistically using the 1–4 scoring scale described previously.

Chi-squared tests of homogeneity were used to evaluate the distribution of one variable against different

levels of another variable.²⁴ A Kruskal–Wallis analysis of variance was used to compare ordinal response scores between two or more independent groups of patients.²⁵ Logistic regression was used to evaluate the functional relationship, if any, between putative explanatory and outcome variables.²⁶ *P*-Values < 0.05 were considered to be statistically significant.

RESULTS

Dogs

Among the 266 dogs were selected for hyposensitization based on the clinical diagnosis of atopic dermatitis and positive reactions in allergy testing (IDST or ELISA), 169 met our criteria for sufficient data to be included in this study. The reasons for exclusion of the 97 dogs not evaluated in the study varied. Hyposensitization was not performed in 45 dogs, hyposensitization was performed for < 1 year in 11 dogs, 36 dogs were unavailable for follow-up either by medical records or by telephone, and 4 dogs had other medical problems that precluded adequate evaluation of response. Hyposensitization was discontinued in one dog because of an anaphylactic-like reaction to the injections.

Breeds

Eighty-two dogs represented 11 different breeds having at least four of each breed. Sixty-six dogs comprised other breeds having 1–3 dogs of each breed. Twenty-one dogs were mixed-breeds.

The Labrador Retriever was the most common breed (*n* = 20) hyposensitized, followed by the Golden Retriever (*n* = 13) German Shepherd Dog (*n* = 8), American Cocker Spaniel (*n* = 7), Doberman Pinscher (*n* = 7), West Highland White Terrier (*n* = 5), Dalmatian (*n* = 5), Bichon Frisé (*n* = 5), English Springer Spaniel (*n* = 4), Dachshund (*n* = 4) and Chinese Shar-Pei (*n* = 4).

Response scores

Thirty-three of 169 dogs (19.5%) exhibited an excellent response. Two dogs were considered 'cured' because treatment was terminated after 1 year of hyposensitization and the pruritus did not recur for a minimum of 2 years. A good response was seen in 55 of 169 dogs (32.5%). Combining groups with scores of 3 and 4, 52% of the dogs showed a good to excellent response to hyposensitization.

Moderate response was seen in 34 of 169 dogs (20.1%). Beneficial response was not seen in 27.8% (47 of 169) of the dogs.

Combining moderate, good and excellent responders, 72% of the dogs benefited from hyposensitization. Approximately one-half (52.6%) of the dogs (moderate and good responders) required additional medical management to control pruritus, whereas in 19.5% hyposensitization alone was sufficient to control the atopic dermatitis.

Response scores in association with different parameters

There were no statistically significant differences in response to hyposensitization among the dog breeds. However, there was a trend for Golden Retrievers to be more likely to respond better, as 9 of 13 had an excellent or good response. The English Springer Spaniel tended to respond less well (three of four did not respond at all and the fourth dog had a moderate response). Four of five Bichon Frisés did not respond, whereas one had an excellent response.

There was no statistically significant difference between the response of male and female dogs. However, there was a trend for males to respond better as there were more excellent responses than expected based on a random distribution of response among male and female dogs (20 dogs vs. an expected number based on random distribution of 15).

Age of onset had no influence on response score. The age when treatment commenced had no significant influence on the response, although dogs that began treatment before 2 years of age had more excellent responses than expected based on random distribution (14 dogs vs. an expected number based on random distribution of 9). However, dogs in this younger group showed the same number of no response to treatment scores as did the other age groups.

The length of time that the dogs had clinical signs of atopic dermatitis before hyposensitization was initiated had no effect on response score. However, there was a trend for dogs that were pruritic for < 1 year before the initiation of hyposensitization to have more excellent responses than would be expected (11 dogs vs. an expected number based on random distribution of 7).

Seasonality of clinical signs had no influence on response. In addition, the seasons when clinical signs of atopic dermatitis began did not influence response to hyposensitization. Further, the season when hyposensitization was initiated had no influence on response.

When clinical features were viewed in association with response scores, dogs without coexisting allergic otitis externa showed a trend for having more excellent responses, although statistical significance was only marginal ($P = 0.0915$). The presence of distal limb pruritus and/or lesions, *Malassezia* dermatitis, and/or *Malassezia* otitis had no influence on response scores.

When concurrent allergies were evaluated in association with response score, dogs with flea allergy dermatitis responded better as they had fewer no response scores ($P = 0.0406$). Concurrent food hypersensitivity had no influence on hyposensitization response scores.

The number of positive reactions were grouped for the purpose of statistical analysis into three groups: 1–10 in 85 dogs; 11–20 in 50 dogs; and > 21 in 34 dogs. The number of positive reactions was significantly correlated with response scores ($P = 0.034$). Dogs that had positive reactions to > 21 allergens had lower response scores: 1 of 34 had an excellent score (expected based on random distribution: 6.6 of 34), whereas 14 of 34 had a no response score (expected based on random

distribution: 9.5 of 34). The number of allergens included in the vials were grouped for the purpose of statistical analysis into three groups: 1–10 allergens in 109 dogs; 11–20 in 46 dogs; and > 21 in 14 dogs. Lower response scores were noted in dogs that were hyposensitized with > 21 allergens in comparison with those that were treated with < 10 allergens ($P = 0.07$).

The specific groups of allergens investigated for association with response to hyposensitization represented those with positive responses on allergy testing and subsequent allergens used for treatment. The exceptions were those allergens noted previously that were not included in the treatment solutions (fleas, insects, sheep's wool and cat epithelia). There was no statistically significant association between response to hyposensitization and the inclusion in the treatment solution of house dust, miscellaneous allergens, dust mites, weeds and moulds. A statistically significant association was not found between response to hyposensitization and a positive response to flea antigen on allergy testing. The following allergens were found to be significantly correlated with the response scores: dogs that were allergic to cultivated plants had very few excellent responses ($P = 0.0007$). Dogs that were allergic to three or more cultivated plants had no excellent response scores at all ($P = 0.0105$). Dogs that were not allergic to grasses responded better, having a higher number of excellent responses ($P = 0.0482$). Dogs that were found to be allergic to trees had significantly fewer excellent response scores ($P = 0.0126$). Dogs that had no positive reactions to insects (not included in the treatment solutions) tended to respond better (24 excellent responses vs. 17 expected based on random distribution, $P = 0.0319$).

There was no significant correlation between excellent, good or moderate response scores and the response time. The response time was found to be significantly correlated only with the number of positive reactions and the number of allergens used in the treatment vials ($P = 0.030$). When the number of the injected allergens was between 1 and 10, the time which elapsed before a response was achieved was significantly shorter ($P < 0.05$) than when > 21 allergens were injected. Thus 1–10 had a mean response time of 7.7 months, with a median of 6 months; 11–20 allergens had a mean of 8.32, median of 8; and > 21 allergens had a mean of 11.6, median of 12.

Twenty-four dogs were tested by ELISA and 135 dogs by IDST. An additional 10 dogs had both tests performed; four of these had their allergen solutions based on the IDST, one had the solution based on serology, and five had their allergen solutions based on both tests. These 10 dogs were excluded from the following statistical comparisons of the two tests' response scores and response times. Among the dogs that were treated based on IDST, the percentages that had excellent, good, moderate and no responses were 19.5, 32, 19.5 and 29, respectively. Of the dogs that were treated based on ELISA results, the percentages that had excellent, good, moderate and no responses were

20, 44, 24 and 12, respectively. The median response time for the dogs treated based on IDST results was 7 months and for those treated based on ELISA was 6 months. Statistically significant differences were not found between these two groups with regard to response scores and response time.

DISCUSSION

Among all the dogs that were selected for hyposensitization, the owners refused treatment in 16% of cases. In three dogs, hyposensitization was not performed because of irrelevant allergens. These dogs were putatively atopic according to their history and clinical signs, and thus possibly allergic to environmental allergens that were not included in the tests, as it is impossible to include every environmental allergen in the allergy tests. If the primary reason for performing allergy tests and identifying allergens is to perform hyposensitization, this was certainly achieved. Primarily, it was the owners who evaluated the response scores and the response time. This evaluation was then obtained either by the history taken during recheck appointments and entered in the medical records, or by telephone calls. Utilizing the owners' evaluations has been done previously^{16,27-29} and found to be reliable.³⁰ The goal of hyposensitization is to achieve relief from the clinical signs to a degree that will be appreciated by the owners.

The overall response rate of 72% was within the range of previous publications.^{1,5,6,27,28,31-33} We had fewer excellent responses than some previous studies.^{2,32,34} This may have been due to the geographical region, as a previous report stated that dogs in California had fewer successful responses.¹ Another explanation is that dogs eventually referred to a university clinic are the more severe or difficult cases. In the comparison of response rates from different data, the subjective criteria for scoring are seldom identical, such that what was found to be 'excellent' by some investigators may be graded as 'good' by others, etc. However, our data show percentages of excellent and no responses which are virtually identical to those found in a retrospective study from Australia (18.5 and 27.4%, respectively).³⁵ That study used the same criteria as ours for excellent responses and no responses.

Although our breeds' responses showed no statistical significance, we did find trends in the response of different breeds to hyposensitization. Golden Retrievers had a tendency to have better responses and English Springer Spaniels and Bichon Frisés had a tendency to have poorer responses. In the results of a survey from Colorado, Scott *et al.* (reported in abstract form)³⁶ found that Retrievers responded less well. Willemse³⁷ found the Boxer and the West Highland White Terrier to be less responsive to hyposensitization. Other reports found no breed differences.^{1,2,16,21,27}

Females and males responded without statistically significant differences, but there was a trend for males to have more excellent scores. The reasons for this are

not clear. One investigator¹⁶ found females to have a higher percentage of 'good to excellent' responses than males. In other studies no sex difference in response was found.²⁷

A trend was not noted for older dogs to have more no responses than good or excellent responses, although this has been suggested previously.^{5,21,27,29,32} There was a trend for dogs that initiated treatment before 2 years of age to have better response scores, although this was not statistically significant. Similar results were found in a study from Australia, in which no differences between responders to hyposensitization vs. nonresponders were found in different ages of onset.³⁵ Furthermore, that study also found a trend for a better response to hyposensitization in dogs that were < 3 years old when treatment began. Dogs older than 6 years of age responded as well as younger dogs and there were no differences in the response to hyposensitization in relation to the age of onset or age when tested. Similar findings have been reported by other investigators.^{16,27} This supports a role for allergy testing and hyposensitization in the treatment of older atopic dogs. In addition, older dogs are less likely to develop new allergies which may interfere with the efficacy of hyposensitization.^{16,17} The amount of time between the onset of clinical signs of CAD and the initiation of hyposensitization had no effect on the response score. However, dogs that had a very short duration of clinical signs (< 1 year) tended to respond better. Perhaps this short duration resulted in a less severe clinical presentation which might have influenced the response score. Other authors have found that the presence of long-term clinical signs resulted in fewer beneficial responses to hyposensitization.^{21,29}

In our study, neither the seasons when the clinical signs occurred nor the season when hyposensitization was initiated had any influence on response. The same finding was reported by other investigators.¹⁶ There are in fact conflicting studies in which dogs with non-seasonal signs predominate in the poor-response group⁵ and others in which the nonseasonal dogs responded much better.¹⁶

The presence of an allergic otitis externa had a slight negative influence on the response scores. If interpreted as a more severe feature of the atopic disease process, this may support the hypothesis that the more severe the clinical presentation, the fewer the beneficial responses. In a retrospective study on response to hyposensitization in Australia the authors also found that dogs that had otitis externa showed more 'no responses', and that dogs with clinical signs of pododermatitis had the same percentage of 'responders' and 'nonresponders', as was found in our study.³⁵

As flea antigens were not included in the allergens selected for hyposensitization, the fact that dogs with concurrent FAD responded better (i.e. had fewer no response scores) may be due to better flea control performed by the owners. Owners that were dedicated enough to perform hyposensitization might also be more dedicated in their flea control management.

Concurrent treatments may have enabled these dogs to reach a level of pruritus that was below their individual allergic threshold, thereby achieving a better response to treatment. Similar findings have been reported,¹⁷ in which atopic and flea-allergic dogs responded better to hyposensitization than atopic dogs that were not flea allergic. Another report found different results, as flea allergy dermatitis was the most common concurrent problem among those dogs with a poor response to hyposensitization.⁵ However, this latter study was performed before modern flea control agents were available.

The study presented here supports previous reports that dogs that were hyposensitized with larger numbers of allergens (> 21) had a statistically significantly lower response rate and a prolonged response time.^{1,2,16,37} There are, however, reports that do not support these findings.^{16,17,21,29} The lack of response to a high number of allergens has been theorized as being because of the dilution of the individual allergen.² Perhaps there is a limited efficacy of the immune system to respond (at least from the standpoint of trying to induce a hyposensitized state) when presented with too many antigens. Differences were not found in the response score or response time between dogs that were positive to 11–20 allergens and those that had fewer than 10 positive reactions. Differences in this lower range of number of allergens have been reported.^{3,16} However, differences in the success rates between dogs receiving < 10 allergens, and those receiving 10 allergens also have been reported.³ It is of interest that one report found that dogs that received a concentration of the allergens $\leq 20\,000$ PNU mL⁻¹ responded better than dogs which received a higher concentration, regardless of the actual number of allergens involved.¹⁶

From the results in this study, positive reactions to three groups of pollen inhalant allergens (cultivated plants, trees and grasses) that were included in the treatments, and one group, insects, that was not included in the treatment, had a significant influence on lowering the response scores. These findings disagree with other reports,^{1,31,32,35} which found that dogs with positive reactions to pollens did better, or to a report in which differences were not found in association with different allergens.²¹ One explanation for our results may be the possible inhibiting effect of mould extracts on pollens when incubated together.³⁸ In our study, moulds were included in a high proportion (60%) of the allergen solutions. Interestingly, hyposensitization to moulds was found to be beneficial in a previous report.³⁹ The ultimate importance of this data may be that if the dog has positive reactions to certain allergens, it may be possible to predict the likelihood of response, thus giving a more accurate prognosis to the owners. Our data showed that dogs that had no positive reactions to insects responded better to hyposensitization. This is similar to results from Australia³⁵ which showed more 'nonresponders' to hyposensitization when there were more strong positive reactions to insects.

The response time found in this study was slightly shorter than in some reports^{4,40} equal to others^{6,37} and longer than others.^{29,41} Having positive reactions to > 21 allergens and receiving > 21 allergens in the hyposensitization solution resulted in both a longer response time and (as noted above) lower response rates. To our knowledge, there are no previously published data that show an influence of the number of injected allergens on the response time. These data illustrate that too great a number of allergens may interfere with the efficacy of hyposensitization. It is also possible that > 21 positive reactions indicate a highly reactive dog, and the lower response rate and the longer time to achieve a response are due to a more severe atopic state. The number of positive reactions thus may be a prognostic indicator for successful hyposensitization.

Thus, better responses to hyposensitization were seen in dogs that had treatment initiated before 2 years of age, as well as in dogs with a short duration of clinical signs (i.e. possibly less severe clinical signs). Conversely, a poorer response as well as a longer response time was seen in dogs with allergic otitis externa and dogs that were hyposensitized with > 21 allergens (possibly more severe clinical signs). It could therefore be hypothesized that it is in the best interest of the patient to diagnose atopy and initiate hyposensitization early in the disease process, before it progresses in severity.

Response scores and time were similar regardless of whether the hyposensitization solutions were based on IDST results or ELISA tests. This supports the findings of other studies^{29,33,36,39,42} although some reports^{6,43} found differences between treatment results according to the two types of tests. The response scores and times are very similar to those published previously.^{27,31} Unfortunately, almost 30% of the dogs did not respond at all, a 50% or greater reduction of the pruritus with or without other treatments was achieved in only 52% of the dogs, and an average of ≈ 7 months was necessary to achieve this effect. These data always raise the question: are we hyposensitizing to the relevant allergens? Testing normal dogs may yield the same positive reactions to certain allergens^{30,44} and there are always potential allergens in the environment which are not included in the tests.⁴⁵ Despite these concerns, hyposensitization is the treatment with the highest success rates.^{1,4}

However, there remains a need for alternative methods of diagnosis and treatment. In order to develop these, a better understanding of the canine disease is necessary: pathogenesis, molecular mediators, etc. In people, newer treatment strategies directed toward manipulation of the immune system to effect a decrease in clinical signs for atopic patients are being developed. These include the use of a permethrin preparation directed against dust mites to put on the skin and bedding,⁴⁶ peptide immunotherapy directed at specific T cells,^{18,47} gene therapy⁴⁸ or the injection of anti-IgE antibodies.⁴⁹ These new strategies may be applicable to dogs and their investigation may add to the knowledge of the canine disease.

Of 217 dogs that began hyposensitization, 36 (17%) were lost to follow-up. This is not as high a drop-out rate in comparison with other studies in which up to 49% of owners²⁹ stopped therapy without consulting the clinicians, or in which 33% of the dogs were lost to follow-up.²¹ There were owners who after several years stopped giving the injections; data regarding the performance of these dogs were not available. Client communication is a key feature in the success of hyposensitization. Diligent follow-up must be done by the clinician, utilizing both telephone calls and re-examination appointments. The main reason for discontinuing hyposensitization is lack of improvement;^{30,41} the clinician thus must be able to help find the reason for failure of the treatment. Some authors² consider the end of the first 6 months of hyposensitization as a critical time when the clinician must see the patient in order to prevent unnecessary discontinuation of the hyposensitization. Other investigators^{34,50} found that if the treatment regime in dogs that were not responding well was modified (frequency, amount injected, etc.), better results could be achieved. In addition to the hyposensitization treatment protocol modified on an individual basis, secondary infections and concurrent allergies must be eliminated or controlled.⁵⁰ Clients must be informed that 1 year of treatment is strongly recommended in order to determine if hyposensitization is successful and that life-long treatment is usually required. In people, long-term hyposensitization does not lead to dysfunction of the immune system or to the development of lymphoproliferative or immunological diseases;⁵¹ presumably the same reassurances may be offered to the owners of atopic dogs.

In previous studies, the allowance of antipruritic medications varied. In a retrospective study, it is virtually impossible to eliminate antipruritic medications, because of the very nature of veterinary medicine's creed of providing relief for animal suffering. However, by acknowledging the use of antipruritic medications in our study, as well as by defining excellent responders as those dogs that no longer needed such medication, we feel we have minimized their influence on the data.

Comparison of studies investigating hyposensitization in canine atopic dermatitis can be difficult because the treatment regimes and/or the allergy tests vary. Using other researchers' data without following the exact hyposensitization regimen used may lead to erroneous assumptions regarding treatment efficacy and misinformation given to the owner. Hyposensitization is a highly demanding and expensive treatment, in which client communication is very important. Owner awareness and compliance are necessary, therefore as much correct information as possible must be given. Ideally, every clinician offering hyposensitization should know their own success rate. It is to be hoped that more published data with various protocols and rates of success may eventually lead to the standardization of hyposensitization procedures.

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Résumé Cent soixante neuf chiens présentant une dermatite atopique ont été désensibilisés pendant au moins un an en fonction des résultats des tests intradermiques (IDT) ou de la sérologie par ELISA. Des résultats excellents (ie: la désensibilisation permet seule le contrôle des signes cliniques), bons (>50% d'amélioration), moyens (<50% amélioration) ou absents (pas de modification des symptômes) ont été observés dans respectivement 19.5, 32.5, 20.1 et 27.8% des cas. L'âge à l'apparition des signes cliniques, l'âge au début du traitement, ou la durée des symptômes ne jouaient aucun rôle pronostique sur l'efficacité de la désensibilisation. Les chiens présentant une dermatite par allergie aux piqûres de puces concomitante avaient statistiquement plus de chance de répondre que ceux présentant une allergie alimentaire concomitante. Bien qu'il n'y ait pas de différence statistiquement significative, les Golden Retrievers et les mâles avaient tendance à être mieux améliorés que les autres races ou les femelles. Les chiens présentant plus de 21 réactions positives aux tests d'allergie, et traités avec plus de 21 allergènes avaient des scores de réponse plus faibles, et répondaient plus lentement au traitement. Une mauvaise réponse a été observée chez les chiens ayant des réactions positives aux plantes, aux herbacées, ou arbres ou aux insectes. Aucune différence significative n'a été observée entre les chiens désensibilisés en fonction des IDT et ceux désensibilisés en fonction des résultats de l'ELISA.

Resumen Se diagnosticó una dermatitis atópica en ciento sesenta y nueve perros, y se trataron con hiposensibilización durante al menos 1 año según los resultados de las pruebas intradérmicas cutáneas (IDST) o en pruebas de ELISA. Se produjeron respuestas excelentes (p.ej. sólo con hiposensibilización se controlaban los síntomas clínicos), buenas (>50% mejora), moderadas (<50% mejora) y sin respuesta (no se modificaron los síntomas clínicos) en el 19.5, 32.5, 20.1 y 27.8%, respectivamente. La edad de inicio de la enfermedad, edad al inicio del tratamiento o la duración de los síntomas clínicos no tenían influencia sobre la respuesta a la hiposensibilización. Los perros con dermatitis alérgica a las pulgas concurrente tenían estadísticamente más probabilidad de responder mejor que los perros con alergias alimentarias. A pesar de no ser estadísticamente significativa, existía una tendencia en los Golden Retriever y en los perros macho a responder mejor que otras razas y los perros hembra, respectivamente. Los perros con más de 21 reacciones positivas en las pruebas de alergia y tratados con más de 21 alérgenos mostraban unos valores de respuesta inferiores, y un lapso de tiempo superior antes de conseguir una respuesta beneficiosa. Los valores de respuesta inferiores se produjeron en perros con reacciones positivas a plantas cultivadas, hierbas, árboles o insectos. No había diferencia en la respuesta a la hiposensibilización entre los resultados de las IDST o los ELISAs.

Zusammenfassung Einhundertundneunundsechzig mit atopischer Dermatitis diagnostizierte Hunde wurden für mindestens ein Jahr mit allergen-spezifischer Immuntherapie basierend auf entweder Intrakutantests oder Enzyme-Linked Immunosorbent Assays (ELISA) behandelt. Exzellente (die Immuntherapie allein kontrollierte die klinische Symptomatik), gute (>50% Besserung), mässige (<50% Besserung) und keine (klinische Symptomatik besserte sich nicht) Wirksamkeit wurde bei 19.5, 32.5, 20.1 und 27.8% der Fälle beobachtet. Das Erkrankungsalter, das Alter zum Zeitpunkt der Immuntherapie oder die Dauer der klinischen Veränderungen hatten keinen Einfluss auf die Wirksamkeit der Immuntherapie. Hunde mit gleichzeitiger Flohbissallergie hatten statistisch eine grössere Besserung als Hunde mit gleichzeitigen Futterreaktionen. Bei Golden Retrievern und Rüden tendierte die Behandlung zur höheren Wirksamkeit, obwohl der Unterschied nicht statistisch signifikant war. Bei Hunden mit mehr als 21 positiven Reaktionen im Intrakutantest, die mit mehr als 21 Allergenen behandelt wurden, war die Behandlung weniger wirksam und es dauerte länger bis zum.

