

THE NORTHWESTERN UNIVERSITY COLONY OF ATOPIC DOGS

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THE occurrence of spontaneous hypersensitivity in animals has been recognized for a number of years^{1, 2} but has been primarily regarded as a curiosity. Investigation of spontaneous hypersensitivity in a dog with ragweed pollen allergy indicated that this type of disease in species other than man might provide a useful model for controlled studies of reactivity to aeroallergens and the effects of certain pharmacologic agents.³ Subsequent studies demonstrated that canine antiragweed serum from a ragweed-sensitive dog had certain established characteristics of human antiragweed serum, which include heat lability at 56° C., failure to demonstrate visible precipitin reactions, and the ability to transfer cutaneous reactivity to normal dogs.⁴ Sufficient quantities of canine antiragweed serum would passively transfer ragweed sensitivity to normal dogs. This phenomenon could be demonstrated not only by immediate wheal and erythema type of skin reactivity, but also by the development of asthma if ragweed antigen or pollen was used as an aerosol challenge, or anaphylaxis if the ragweed antigen was injected intravenously.⁴ Passively sensitized dogs challenged intravenously showed pathologic changes characteristic of those previously described in anaphylaxis in dogs actively sensitized to heterologous serum.⁵ The transferring factor in the serum from the ragweed-sensitive dog was characterized to some extent by zone electrophoresis and salting out procedures⁶ and appeared to have characteristics similar to those described for human antiragweed sera.⁷ The circulating levels of histamine in the passively sensitized, intravenously challenged dogs have been measured and correlate to some extent with clinical and pathologic changes observed.⁶

The apparent usefulness of dogs with spontaneous pollen allergy as laboratory models of human pollen allergy for studies that cannot be conveniently carried out in human allergic patients encouraged the search for a group of these animals. A comparative study of the clinical manifestations and the immunopathology should provide similarities and differences which could lead to a better understanding of the atopic type of hypersensitivity. This report describes the characteristics of the dogs studied to the present and the establishment of a small colony of allergic dogs in residence at Northwestern University.

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MATERIALS AND METHODS

Collection of the Group of Allergic Dogs.—Dogs studied were those reported by interested veterinary physicians. All dogs were private pets and available only for limited study. Because dogs with symptoms unrelated to allergic disease were occasionally referred for study of allergic disease, certain criteria were established in order to determine whether a dog should be included as having true spontaneous atopic type of hypersensitivity. Criteria for diagnosis of allergic disease were, therefore, limited initially to ragweed allergy because of the importance of this aeroallergen in the Midwest and the well-defined pollen season. Dogs with definite symptoms during the ragweed season were tested with ragweed pollen antigen by intracutaneous tests. Positive reactions consisted of wheal and erythema reactions which could be made markedly visible by simultaneous intravenous injection of Evan's blue dye.⁴ Sera from dogs with positive cutaneous reactions were used for passive transfer of cutaneous reactivity. Dogs were not included in the group unless the above criteria were met. Four dogs were obtained for permanent residence as the colony of allergic dogs. Since more extensive studies on these dogs could be done, 2 additional criteria were established for inclusion in this group. These were the development of acute respiratory symptoms during controlled exposure to ragweed pollen antigen in a chamber with the use of a method previously described,³ and the passive transfer of anaphylaxis to a normal dog with serum from each of the ragweed-sensitive dogs.⁴

Antigens.—Pollen antigens were extracts of whole pollen prepared as water-soluble extracts,⁸ except for purified ragweed antigen* used for certain studies.

Serum Fractionation.—The fractionation of serum by starch block electrophoresis and ammonium sulfate precipitation was done in the manner previously described for canine antiragweed serum.⁴

In Vitro Antibody Tests.—Tanned red blood cell (TRBC) hemagglutination reactions were done by the method of Stavitsky⁹ with the use of crude ragweed antigen or purified ragweed antigen. Coprecipitation of I¹³¹-trace-labeled purified ragweed antigen was done using the method described for coprecipitation studies of human antisera against I¹³¹-labeled horse serum albumin.¹⁰

RESULTS

Various methods of finding dogs allergic to ragweed were attempted. Testing all dogs brought to a medical school for various purposes with ragweed antigen was not successful in producing subjects for study. All sensitive animals were obtained through the cooperation of interested veterinary or medical physicians. A total of 12 dogs with seasonal symptoms during the pollination of ragweed and positive cutaneous reactions to ragweed antigen were found. The sera of all dogs transferred cutaneous reactivity to ragweed antigen to the skin of normal dogs.

The symptoms of the dogs with cutaneous reactivity to ragweed varied in

*Supplied by Dr. T. P. King, Rockefeller Institute, New York.

both the type of clinical manifestation and severity of symptoms. A major problem was pruritic dermatitis, generally the reason that the dog was brought to the veterinary physician. Conjunctivitis was often an associated complaint, and sneezing and coughing were occasionally mentioned. Historical details were often difficult to obtain and a complete definition of the extent and severity of the clinical manifestations of allergy in dogs was not possible.

From the group of 12 dogs studied it was possible to collect 4 of them to form a permanent colony at Northwestern University Medical School. Some characteristics of this group are outlined in Table I.

Sensitivity to ragweed pollen was present in all dogs and dermatitis was a major symptom in all dogs. This may reflect the manner of selection of cases

TABLE 1. PERMANENT COLONY OF ALLERGIC DOGS

Dog		1	2	3	4
Breed		Fox Terrier	English Setter	Welsh Terrier	Wirehaired Terrier
Sex		Female	Male	Female	Female
Age (years)		7	10	3	6
Duration of symptoms (years)		6	9	2	Unknown
Clinical symptoms during ragweed season		Dermatitis Rhinitis Conjunctivitis Cough	Dermatitis Rhinitis Conjunctivitis Cough	Dermatitis Cough	Dermatitis
Seasonal relation of symptoms		Limited to ragweed season	Perennial	Limited to ragweed season	Limited to ragweed season
Intracutaneous tests to aeroallergens	Tree	Positive	Positive	Negative	Negative
	Grass	Positive	Positive	Negative	Negative
	Ragweed	Positive	Positive	Positive	Positive
	Mixed mold	Negative	Negative	Negative	Negative
	House dust	Negative	Negative	Negative	Negative
Symptoms during exposure to aerosolized antigens	Tree	Asthma Conjunctivitis	Asthma Conjunctivitis	None	None
	Grass	None	Asthma Conjunctivitis	None	None
	Ragweed	Asthma Conjunctivitis	Asthma Conjunctivitis	Asthma Conjunctivitis	Asthma Conjunctivitis
Passive transfer of cutaneous reactivity to ragweed to normal dog skin		Positive	Positive	Positive	Positive
Passive transfer of anaphylactic sensitivity to ragweed to normal dogs		Positive	Positive	Positive	Positive

TABLE II

	DOG				NORMAL DOG SERA
	1	2	3	4	
TRBC hemagglutination reaction*	1,600	3,200	200	2,560	20
Coprecipitation† of I ¹³¹ ragweed antigen	70	31	0	60	0.5
Dilution of antisera resulting in positive transfer to normal dog skin‡	125	25	Undiluted	125	Negative

*Recorded as reciprocal of highest dilution giving positive reaction.

†Recorded as per cent binding of 0.0012 μ g N of I¹³¹-labeled purified ragweed antigen by 0.05 ml. of antiserum.

‡Recorded as reciprocal of highest serial fivefold dilution giving positive passive transfer to normal dog skin.

as well as the major type of clinical manifestations and most frequent etiologic antigen. Sensitivities to pollen antigens other than ragweed antigen occurred, demonstrated by both cutaneous reactivity and symptoms following controlled exposure to the aerosolized antigen. In this group of 4 dogs, ragweed pollen sensitivity could be used as a major example of hypersensitivity disease and sera collected from the dogs was used for in vivo and in vitro studies. Sera from these dogs passively transferred cutaneous and anaphylactic sensitivity to ragweed pollen antigen. The ability of sera to transfer cutaneous reactivity, as demonstrated by the titrations of sera using serial fivefold dilutions of each serum, varied with different dogs. Initial results with the transfer of anaphylaxis by these antisera suggested a correlation between the dilution of the antiserum capable of transferring cutaneous reactivity and amount of antiserum necessary to produce passive anaphylaxis.

Studies of the combination of canine antiragweed sera with ragweed antigen by two techniques are recorded in Table II and can be compared with the serial dilution resulting in positive passive transfer reactions. No definite correlations could be made between severity of symptoms and TRBC hemagglutination titers. The latter titers could be correlated as much with age of the dogs as with ability of sera to transfer skin reactivity. The binding of I¹³¹-trace-labeled antigen could be correlated to some extent with ability to transfer skin reactivity but the series of animals is not sufficiently large to provide definite information at present. Sufficient quantities of canine antisera have not been available for extensive studies and correlation of passive transfer of skin reactivity with the ability of canine antiragweed sera to transfer anaphylaxis to normal dogs. However, initial results suggest that less of the antisera which, at higher dilutions, transfers skin reactivity is required to transfer anaphylactic sensitivity to normal dogs.

DISCUSSION

The occurrence in 12 dogs of symptoms during the ragweed season associated with cutaneous reactivity and circulating antibody capable of giving cutaneous passive transfer reactions suggests that this type of hypersensitivity in dogs is not rare. Studies on the colony of dogs in residence indicate that canine hyper-

sensitivity is a useful model for controlled studies of hypersensitivity not possible in man because of either convenience or safety.

The establishment of ragweed pollen sensitivity and certain other aero-allergen sensitivities does not imply that pollen sensitivity is the major cause of allergic disease in dogs. Other antigens, as flea antigens, may be of greater clinical importance, and variations depending on geographic location undoubtedly occur. The importance of other inhalant, ingestant, or contact allergens as etiologic agents in canine atopic disease requires further study.

Clinical manifestations of seasonal or perennial allergy in dogs observed in the present studies are conjunctivitis, rhinitis, asthma, and dermatitis. The significance of the dermatitis as a clinical problem has been the major difference between human and canine allergic disease observed to the present. The dermatitis consists of an intensely pruritic eczematoid reaction which was most often the major complaint of the owners of pets. Dogs with ragweed allergy and severe dermatitis during the ragweed season developed acute respiratory symptoms when exposed in the laboratory to ragweed pollen or ragweed pollen extracts in acute experiments. Short-term exposure to ragweed antigen by aerosolization did not result in dermatitis. The reason for the greater incidence of dermatitis in dogs as contrasted with man has not been established. While this may indicate a major species difference in clinical manifestations, irritation from scratching, causing inoculation of antigens or associate contact allergy, are other possibilities for the occurrence of dermatitis as a major clinical manifestation in dogs.

SUMMARY

Twelve cases of dogs with spontaneous allergic disease to pollen antigen are reported. Four of these dogs have been established as a permanent colony for the comparative study of canine and human allergic disease.

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