

# A prospective study on canine atopic dermatitis and food-induced allergic dermatitis in Switzerland

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set representing more than 85% of all Swiss dogs. The study, which was carried out during 1 year in several practices and teaching hospital in Switzerland, describes a group of 259 allergic dogs, determines breed predisposition for atopic dermatitis and food-induced allergic dermatitis, compares the clinical signs and features of both conditions, and outlines the clinical picture of five frequently affected breeds.

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## Introduction

Canine atopic dermatitis (CAD) is a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens.<sup>1</sup> Genetic, immunological and environmental factors are consequently associated with the initial development and flares of the condition.<sup>2,3</sup> Food components may also trigger flares of CAD and, consequently, some cases of cutaneous adverse food reactions (CAFR) manifest clinically as CAD.<sup>4</sup> Canine AD *sensu lato* (CADsl) should therefore be regarded as a clinical diagnosis of a disease that may be triggered by several factors, including food components. One must, however, keep in mind that not all cases of CAFR exhibit clinical signs of CAD nor may have immunological causes.<sup>5</sup> For the purposes of clarity in the rest of this article, we will use the term food-induced allergic dermatitis (FIAD) to describe cases of CAFR exhibiting clinical signs of CAD and the term CAD *sensu stricto* (CADss) for cases exhibiting clinical signs of CADsl which are not responsive to an elimination diet.

The clinical signs of CADsl are quite variable and there is no pathognomonic sign or feature that indicates the presence of the disease. Some typical findings have, however, been grouped into lists of criteria having a strong association with CAD.<sup>6,7</sup> These lists should be considered in evaluation of pruritic dogs, keeping in mind that none of these sets of features are fully accurate for the diagnosis of CAD.<sup>8</sup> One must thus rule out resembling diseases such as infestations with ectoparasites or primary bacterial infections. To further complicate the diagnosis, several factors such as breed, duration of the disease, and presence of secondary infections may influence the clinical picture.<sup>8-10</sup> In order to better define the clinical signs and features of CAD, and especially, breed predispositions, several teams have described populations of atopic dogs.<sup>11-14</sup> Unfortunately, predispositions have often been determined without any reference to the basic population, or in comparison with the hospital populations, which induces bias.

### What is known about the topic of this paper

- Atopic dermatitis and cutaneous adverse food reactions are common skin conditions in dogs.
- Food components may trigger flares of atopic dermatitis and some cases of cutaneous adverse food reactions manifest clinically like atopic dermatitis.
- Breed predispositions for atopic dermatitis have been demonstrated but may vary depending on geographical regions.

### What this paper adds to the field of veterinary dermatology

- This is the first attempt to draw a population of allergic dogs from a whole canine population and to compare their characteristics.
- Swiss breed predispositions for atopic dermatitis but also for adverse food reactions are statistically demonstrated.
- An attempt is made to determine breed phenotypes of allergic dogs in Switzerland.

## Abstract

**Canine atopic dermatitis *sensu stricto* and food-induced allergic dermatitis are common canine skin conditions, which are often considered clinically undistinguishable. Several attempts have been made to describe populations of atopic dogs and determine breed predisposition but the results were often biased by the use of hospital populations as control group. The present study aims to describe a population of Swiss atopic and food-allergic dogs and to compare it with a data**

The goal of the present study was to determine the clinical features of a population of Swiss dogs exhibiting clinical signs of CADs and FIAD. Taking advantage of the existence in Switzerland of the Animal Identity Service (ANIS), which claims to have registered more than 85% of all Swiss dogs, we have compared this population with atopic dogs diagnosed in eight different Swiss veterinary clinics or teaching hospitals by 11 dermatologically experienced veterinarians or specialists in the field. We have additionally compared clinical symptoms of dogs with CADs versus dogs with FIAD and attempted to determine breed-associated phenotypes in five frequently affected breeds.

## Material and methods

### Swiss ANIS population

Date of birth, sex and breed of all dogs registered at ANIS were collected. As all owners of dogs living in Switzerland are required by law to register their pet at ANIS, one may assume that the database is representative of the whole Swiss canine population.

### Patient selection and diagnostic evaluation

Eleven veterinarians with extensive experience in veterinary dermatology, working in eight different veterinary clinics or teaching hospitals throughout Switzerland, included cases of CADs and FIAD for over 1 year (June 2006 to June 2007).

Dogs were included based on fulfilment of the Willemse's criteria.<sup>6</sup> Similar dermatoses such as ectoparasites and primary bacterial infections were also ruled out.

In order to differentiate between FIAD and CADs, an elimination diet was carried out with home-cooked diet (horsemeat with potatoes) or, alternatively, selected commercial food (hypoallergenic diet<sup>1</sup>), for over 6 weeks. Dogs that improved during the trial were all challenged with previously fed foods. A definitive diagnosis of FIAD was made based on the recurrence of clinical signs upon food challenge.

### Outcome evaluations

Breed and sex of selected dogs were compared to the ANIS population. The analysis was first made for the whole population of CADs dogs, then for CADs and FIAD dogs, separately. The following clinical signs and features were evaluated by the investigators in all selected dogs and recorded on a standard form: age at onset, presence of pruritus 'sine material' at onset, seasonality (defined as occurrence or exacerbation of the signs during spring or summer), localization of the lesions, presence of secondary bacterial and yeast infections (assessed by cytological examination), presence of otitis externa, onset of otitis externa before or after other clinical signs, interdigital fistulae and/or interdigital pyoderma, pyotraumatic dermatitis, urticaria, angioedema, seasonal conjunctivitis or sneezing, gastrointestinal disturbances (diarrhoea, vomiting, tenesmus, soft stools, increased faecal frequency: information collected by questioning the owners), oily or dry seborrhea, and response to glucocorticoid therapy.

In order to uncover potential differences between CADs and FIAD dogs, both populations were compared. As some reports mentioned that young atopic dogs first developed seasonal signs, an attempt was made to correlate age with seasonality.

In CADs dogs, the frequency of seasonality in each age group (< 6 months of age; < 1 year old; < 3 years old; > 3 years old) was studied and compared to the other age groups.

Additionally, five breeds (West Highland white terrier (WHWT), German shepherd dog, boxer, Labrador and golden retriever) were selected for further evaluation because of the high number of affected dogs. The same clinical features were compared in an attempt to determine breed-associated phenotypes.

<sup>1</sup>Royal Canin, Sensitivity Control with Capelin and Tapioca or Hypoallergenic diet from Royal Canin or Hypoallergenic diet from Purina or from Hill's z/d or from Swiss Animal Food Sensidog.

## Statistical analysis

Data analysis was performed with GraphPad Prism version 4.0 (GraphPad Software, San Diego, CA, USA). Proportions of the above listed clinical signs and features were first compared, grouping dogs with CADs and FIAD versus the healthy canine population, and then separately considering the two diseases. Proportions were also compared between dogs affected by CADs or FIAD. Analysis was achieved with chi-square test or Fisher's exact test followed by Bonferroni correction. Significance was set at a *P*-value of  $\leq 0.05$ . Significance without Bonferroni correction is sometimes mentioned in tables or in the text, when the authors considered that this feature may provide some valuable information, i.e. trends. The determination of breed-associated phenotype was carried out with the same statistical tools. Each breed was compared to the whole population of affected dogs.

## Results

### ANIS Swiss population

The original Swiss dog dataset consisted of 418 422 microchipped dogs.

There were 205 543 (50.6%) males, 211 786 (49.1%) females. The sex was not determined for 1147 (0.3%).

### Study population

The study ran from June 2006 to June 2007 and a total of 259 allergic dogs were included. Of these 259 affected dogs, 183 (70.7%) suffered from CADs while 65 (25.1%) were afflicted with FIAD and 11 dogs (4.2%) responded only partially to an elimination diet or were diagnosed as suffering from both conditions.

### Comparison between the study population and the ANIS population

Breed predispositions have been studied for the whole study group (*n* = 259), for CADs dogs (*n* = 183) and for FIAD dogs (*n* = 65); results are summarized in Table 1a–c. The following breeds are predisposed for CADs: WHWT, boxer, French bulldog, Vizsla, bullterrier and Rhodesian ridgeback. Additionally, pugs and Dalmatians were over-represented in the study group but without any significance after Bonferroni correction. When one considers CADs, WHWT, boxer, French bulldog, bullterrier, Vizsla and basset are predisposed. Once more, Dalmatians were also over-represented in this group. On the other hand, WHWT, boxers, Rhodesian ridgebacks and pugs were predisposed for the development of FIAD. Additionally, German shepherd dogs were at higher risk for the development of FIAD when the data were considered without Bonferroni corrections.

The Yorkshire terrier, standard poodle, Bernese mountain dog, Appenzeller dog and border collie breeds had reduced incidences of CADs. There were 122 female (47%) and 137 male dogs (53%) in the study group. These percentages were not statistically significantly different when compared to the ANIS population. It is, however, worth noting that male Labradors have a tendency to be overrepresented (17 of 22, *P* < 0.07) in the CADs group.

### Comparison between CADs and FIAD dogs

Clinical signs and features were analysed in both groups and are presented in Table 2. Statistical differences were found for age at onset, seasonality, gastrointestinal signs and the occurrence of yeast infections.

Sixteen percent of the dogs in the CADs group exhibited clinical signs before 1 year of age and 78% were younger

**Table 1.** (a) CAD dogs (whole study group): frequently affected breeds

Breed	Patient population		Swiss population	
	Number	Percentage	Number	Percentage
West Highland white terrier**	30	11.6	8 435	2
Mixed	30	11.6	34 124	8.2
Labrador	22	8.5	34 596	8.3
Boxer**	18	6.9	4 675	1.1
Golden retriever	18	6.9	18 385	4.4
German shepherd	15	5.8	18 472	4.4
French bulldog**	6	2.3	1 266	0.3
Bullterrier**	5	1.9	513	0.1
Dalmatian*	5	1.9	2 854	0.7
Jack Russel terrier	5	1.9	12 973	3.1
Vizsla**	5	1.9	360	0.1
Rhodesian ridgeback**	4	1.5	949	0.3
Chihuahua	4	1.5	3 732	0.9
Pug*	4	1.5	1 611	0.4

\*Statistical significance without Bonferroni correction ( $P < 0.05$ ).

\*\*Statistical significance with Bonferroni correction ( $P < 0.05$ ).

(b) Canine atopic dermatitis *sensu stricto* (CADss): frequently affected breeds

Breed	Patient population		Swiss population	
	Number	Percentage	Number	Percentage
West Highland white terrier**	22	12	8 435	2
Mixed	21	11.5	34 124	8.2
Labrador	15	8.2	34 596	8.3
Boxer**	15	8.2	4 675	1.1
Golden retriever	12	6.6	18 385	4.4
German shepherd	7	3.8	18 472	4.4
French bulldog**	5	2.7	1 266	0.3
Bullterrier**	4	2.2	513	0.1
Dalmatian*	4	2.2	2 854	0.7
Jack Russel terrier	4	2.2	12 973	3.1
Vizsla**	4	2.2	360	0.1
Basset**	3	1.6	297	0.1

\*Statistical significance without Bonferroni correction ( $P < 0.05$ ).

\*\*Statistical significance with Bonferroni correction ( $P < 0.05$ ).

(c) Dogs with food-induced allergic dermatitis: frequently affected breeds

Breed	Patient population		Swiss population	
	Number	Percentage	Number	Percentage
West Highland white terrier**	8	12.3	8 435	2
Mixed	6	9.2	34 124	8.2
Labrador	6	9.2	34 596	8.3
German shepherd*	6	9.2	18 472	4.4
Golden retriever	5	7.7	18 385	4.4
Pug**	4	6.2	1 611	0.4
Boxer**	3	4.6	4 675	1.1
Rhodesian ridgeback**	3	4.6	949	0.3

\*Statistical significance without Bonferroni correction ( $P < 0.05$ ).

\*\*Statistical significance with Bonferroni correction ( $P < 0.05$ ).

than 3 years at clinical onset of disease. In the FIAD group initial clinical symptoms occurred before 1 year of age in 48% and before 3 years of age in 83%. The former figure is statistically significant ( $P < 0.03$ ) compared to the CADss group.

As expected, seasonality was not present in FIAD dogs. On the contrary, 64 (35%) dogs with CADss exhibited seasonality. Fifty-nine (92%) of the seasonally affected dogs exhibited clinical signs in spring and/or summer and five (8%) during winter. There was no correlation between the age of the affected dogs and the seasonality.

Furthermore, the occurrence of gastrointestinal signs and yeast infections was far more frequent in FIAD dogs than in CAD dogs ( $P < 0.0001$  and  $P < 0.0002$ , respectively).

#### Attempts to determine breed phenotypes

In an attempt to uncover breed-associated phenotypes, the clinical features and signs of the five most frequently affected breeds were compared. For each breed, the number of dogs affected with one specific feature was compared with the whole group. Results are summarized in Table 3.

**Table 2.** Clinical signs and features of dogs with canine atopic dermatitis *sensu stricto* (CADss) and dogs with food-induced allergic dermatitis (FIAD)

Clinical sign	CADss dogs (n = 183)		FIAD dogs (n = 65)	
	Number	Percentage	Number	Percentage
Cortico-responsive pruritus	153	84	48	74
Chronic or recurrent otitis externa	80	44	36	55
→First episode before other signs	43	23	22	34
←First episode concomitant or after	29	16	10	15
Previous episode of hot spots	18	1	7	11
Concomitant interdigital fistula	24	13	14	22
Chronic diarrhoea/vomiting	18	1	20*	31
Affected front feet	137	75	43	66
Affected hind feet	126	69	42	65
Affected axillae	117	64	34	52
Affected abdomen/inguinal areas	119	65	34	52
Affected lips	61	33	23	35
Affected eyelids	50	27	15	23
Affected elbow	39	21	16	36
Affected dorso lumbar	28	15	16	36
Chronic bacterial infection	118	64	43	66
Chronic yeast infection	36	20	28*	43

\*Statistical significance with Bonferroni correction ( $P < 0.05$ ).

**Table 3.** Frequency of clinical signs and features of four canine atopic dermatitis *sensu lato* (CADsl) frequently affected breeds: Statistical comparison with the whole group of allergic dogs (259 dogs)

Clinical sign percentage	WHWT n = 30	Labrador retriever n = 22	Boxer n = 18	Golden retriever n = 18	German shepherd n = 15
Age at onset					
< 1 year old	27	36	56	33	53
< 3 years old	73	82	89	67	93
> 3 years old	27	18	11	33	7
Cortico-responsive pruritus	77	77	67	89**	87**
Pruritus sine materia at onset	67	55	56	61	67
Chronic or recurrent otitis externa	60	45	67	50	60
Conjunctivitis	20	32	33	11	40
Seasonality	27	36	11	28	13
Seborrhea oleosa	27**	5	11	0	40**
Previous episode of hot spot	7	27**	0	28**	7
Interdigital fistula	20	32**	11	6	13
Affected front feet	90	77	83	50*	80
Affected hind feet	83	77	83	56	73
Affected axillae	57	55	44	83	67
Affected abdomen/inguinal	60	50	72	72	73
Affected genitalia/ventral tail	53	32	28	56	47
Affected lips	43	23	39	50	47
Affected dorso lumbar	37**	9	0	33	0
Secondary bacterial infections	90**	64	72	67	100**
Secondary yeast infections	67**	36	83**	28	67**

\*Statistical significance without Bonferroni correction ( $P < 0.05$ ).

\*\*Statistical significance with Bonferroni correction ( $P < 0.05$ ).

WHWT, West Highland white terrier.

Golden retriever and German shepherd dogs seemed to be more responsive to glucocorticoid therapy than the other breeds. Furthermore, WHWT and German shepherd dogs showed seborrhea oleosa in association with CAD significantly more often compared to the whole group. This feature could explain the predisposition of these breeds to both yeast and bacterial infections. Boxers were also predisposed to yeast infections. Regarding distribution, WHWT were more often affected with pododermatitis of the front feet, whereas golden retrievers were less often affected. WHWT and golden retrievers sometimes

presented with lesions on the dorso-lumbar areas. Labrador and golden retrievers were more often affected by pyotraumatic pyoderma, whereas WHWT were less often affected than other breeds. Labrador retrievers also frequently presented with interdigital fistulae in association with CADsl.

## Discussion

We have taken advantage of the existence of an animal database to carry out this cross-sectional study of Swiss

allergic dogs. This study contributes to describe some breed-associated allergic phenotypes to confirm that only some minor differences exist in the clinical presentation of dogs suffering FIAD and CADs and to determine breed predispositions.

Reliable evaluation of breed predispositions for veterinary diseases is complicated by the fact that the population at risk is often unknown. Several studies have, however, addressed the question of breed predisposition for CAD.<sup>3</sup> Some studies only mentioned the most frequently represented breeds while some others have been based on a comparison between atopic dogs and the hospital or insurance population.<sup>9,11,12,14–18</sup> The former do not present any statistical analysis and the latter may be biased by the absence or the underrepresentation of healthy dogs. One single study is based on a large population of insured dogs but contains another potential bias: the authors did not make the diagnosis of CAD themselves but referred to the diagnosis of general practitioners, who may have used variable inclusion criteria.<sup>12</sup> To further complicate the analysis, predisposed breeds may vary by geographical areas.<sup>19,20</sup> Some breeds such as WHWT, boxers, golden retrievers or Labrador retrievers are, however, mentioned in virtually all these studies. Some others such as German shepherd dogs seem to be predisposed for CAD only in some geographical regions.

The Swiss dog population is unique in that all dogs' owners are required by law to microchip or tattoo their dogs and to register them in a central database. The data set is consequently likely to be representative of the population of Swiss atopic dogs. The authors, who worked in eight different practices throughout Switzerland, have recorded the clinical features and signs of confirmed cases of CADs and/or FIAD. Interestingly, three breeds that are often considered overrepresented do not appear to be predisposed in our study: Labrador, golden retriever and German shepherd dogs. It is worth noticing, however, that dogs belonging to these breeds were frequently diagnosed with CADs and/or FIAD because they are also very popular breed in Switzerland.

Our study confirms that some breeds, such as WHWT, boxer, French bulldog or bullterrier, are also predisposed to CAD in Switzerland. To the best of our knowledge, breed predisposition for FIAD have not been firmly demonstrated previously, even if some breeds were considered at risk: boxer, cocker and Springer spaniel, collies, Dalmatian, German shepherd dogs, Lhasa apso, Miniature schnauzer, retriever, shar pei, dachshund and WHWT.<sup>5,21–23</sup> In Switzerland, WHWT, pugs, boxer, Rhodesian ridgeback, and to a lesser extent, German shepherd dogs are predisposed breeds for this condition. Twenty-five percent of our study population were affected by FIAD. Several other studies have shown that 7–26% of dogs with clinical signs compatible with CADs or FIAD were affected by FIAD.<sup>2,24–30</sup> Our results, even if relatively high, are completely in line with the previous reports. It is also worth noticing that using commercial diets in some dogs could have reduced the number of FIAD diagnoses as well as the number of dogs with both FIAD and CADs. Our study has also confirmed that CADs and FIAD are often clinically indistinguishable. FIAD is sometimes said to be less responsive to corticosteroid treatment but this assumption was not confirmed in our

study.<sup>21,24</sup> On the other hand, our study has demonstrated that FIAD dogs are prone to yeast infections and gastrointestinal signs. The latter feature was already frequently recorded but the former was never shown and probably reflects differences in breed predisposition. Last but not least, our study confirms that FIAD dogs are usually younger than CADs dogs at onset of clinical disease.

In contrast with FIAD, clinical signs of CADs can be seasonal or nonseasonal. The seasonality rate found in this investigation was higher (37%) than reported in the literature.<sup>9,11,13,31</sup> However, initial signs of CADs are reported to be seasonal in 42–75% of dogs.<sup>19,32,33</sup> We were not able to confirm this assumption. Canine AD is often considered as a good model for its human counterpart, which is known to be associated with several mutations.<sup>34</sup> It seems consequently logical and tempting to hypothesize that the variability of the clinical features presented by atopic patients could be due to variable genetic make-ups. In this regard, we have recorded the features of CAD dogs belonging to the five most frequently affected breeds. Although the number of dogs in each group is too low to draw some definitive conclusions, this study outlines the clinical pictures of five CAD-affected breeds.

The study contributes to better characterize the population of Swiss allergic dogs. Further studies, including more animals in a larger geographical area, are however, required to assess whether our findings may be extended to other groups and to better define breed-associated phenotypes.

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**Résumé** La dermatite atopique canine au sens strict et l'allergie alimentaire sont des maladies fréquentes chez le chien, qui se ressemblent souvent. Différents essais ont été réalisés pour décrire les populations de chiens atopiques et pour déterminer une prédisposition raciale, mais les résultats sont souvent biaisés par l'utilisation de populations de malades comme groupes contrôles. Cette étude vise à décrire une population de chiens suisses atopiques ou allergiques alimentaires et de les comparer avec une base de données correspondant à 85% de tous les chiens de Suisse. Cette étude, qui a été réalisée dans plusieurs cliniques et écoles vétérinaires sur une période de un an, décrit un groupe de 259 chiens allergiques, détermine les prédispositions raciales pour la dermatite atopique et l'allergie alimentaire, compare les signes cliniques des deux maladies et souligne les signes cliniques chez cinq races fréquemment atteintes.

**Resumen** La dermatitis atópica canina en sentido estricto y la dermatitis alérgica inducida por alimentos son procesos comunes en la piel de perros, tradicionalmente no diferenciables en base a presentación. Se han producido diversos intentos de describir poblaciones de perros atópicos y determinar una predisposición de raza, pero los resultados eran a menudo desviados por el uso de animales de hospitales de referencia como grupos control. Este estudio describe una población de perros Suizos atópicos y perros con dermatitis alérgica a alimentos y los compara con una población que representa más del 85% de todos los perros suizos. El estudio, llevado a cabo durante un año en varios hospitales clínicos y de universidades, describe un grupo de 259 perros alérgicos, determina la predisposición a dermatitis atópica y alimentaria de diferentes razas, y compara los signos clínicos y características de ambas condiciones, resaltando el cuadro clínico de las cinco razas afectadas con mayor frecuencia.

**Zusammenfassung** Die canine atopische Dermatitis im engeren Sinn und die durch Futtermittel induzierte allergische Dermatitis stellen häufige Hautprobleme beim Hund dar, die oft klinisch als nicht unterscheidbar gelten. Es sind bereits mehrere Versuche unternommen worden, um Populationen von atopischen Hunden zu beschreiben und eine Rassenprädisposition zu bestimmen. Die Ergebnisse waren jedoch oft durch die Verwendung einer Klinikpopulation als Kontrollgruppe einseitig beeinflusst. Das Ziel der vorliegenden Studie war es, eine Population von atopischen und Futtermittel-allergischen Hunden aus der Schweiz zu beschreiben und sie mit einem Datensatz, welcher mehr als 85% aller Hunde der Schweiz repräsentierte, zu vergleichen. Die Studie, die im Laufe eines Jahres in verschiedenen Praxen und Universitätstierkliniken der Schweiz durchgeführt wurde, beschreibt eine Gruppe von 259 allergischen Hunden, bestimmt die Rassenprädisposition für die atopische Dermatitis und die Futtermittel induzierte allergische Dermatitis, vergleicht die klinischen Symptome und besonderen Merkmale beider Krankheitsbilder und fasst das klinische Bild von fünf häufig betroffenen Rassen kurz zusammen.