

Prevalence of adverse food reactions in 130 dogs in Italy with dermatological signs: a retrospective study

OBJECTIVES: To determine the prevalence of adverse food reactions (AFRs) in dogs with dermatological signs presented to the referral dermatological clinic of the University of Milan.

METHODS: The medical records of dogs with dermatological signs were reviewed. Prevalence of AFRs was calculated. Owner and clinician pruritus scores were compared. Breed, sex and age predisposition were statistically tested, as was the association between AFR and selected clinical features.

RESULTS: The prevalence of AFRs in dogs with dermatological signs was 12% (16 of 130). AFR was diagnosed in 26% of dogs with allergic disease and 48% of those subjected to a dietary trial. There was a significant association between AFRs and early onset of clinical signs (<1 year) (OR=3.8; P=0.0221, 95% CI=1.27 to 11.16). There was a significant association between AFRs and both otitis externa (OR=5.9; P=0.0015, 95% CI=2 to 17.9) and perianal fistula (OR=26.1; P=0.0058, 95% CI=2.52 to 269.4), although all dogs with perianal fistulas were German shepherd dogs.

CLINICAL SIGNIFICANCE: The prevalence of AFRs in the study population was higher than most reported values. Further studies are warranted to investigate the true prevalence of AFR and its possible association with perianal fistula and other potential markers.

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INTRODUCTION

Adverse food reactions (AFRs) in dogs are common but poorly understood (Chesney 2002). These reactions include food allergy, food intolerance and non-allergic food hypersensitivity (Anderson 1986, Johansson and others 2004). AFRs in dogs can cause a variety of dermatological signs, including pruritus, papules, erythema, scaling, excoriations and erosions, pyotraumatic dermatitis, epidermal collarettes, otitis externa, pododermatitis and seborrhoea (Walton 1967, Harvey 1993, Rosser 1993, Denis and Paradis 1994, Scott and others 2001).

The veterinary literature is equivocal on the true incidence and prevalence

of AFRs (Verlinden and others 2006). Canine AFRs were considered responsible for only 1 to 5% of all canine skin disease (Walton 1967, Carlotti and others 1990, Denis and Paradis 1994, Scott and others 2001, Wilhelm and Favrot 2005) and 10 to 15% of all canine allergic dermatoses (Carlotti and others 1990, Scott and others 2001). Recently, AFRs were considered the sole cause of skin disease in 17 to 35% of dogs with non-seasonal pruritus (Chesney 2002, Biourge and others 2004, Loeffler and others 2006).

A systematic review of the literature highlighted many difficulties in accurately estimating the prevalence of this disease (Chesney 2001). Many published reports did not report the population size from which the dogs were drawn, the number of dogs that were removed from the study or the criteria used to quantify improvement (Chesney 2001). In addition, accurate diagnosis remains a challenge. A dietary elimination trial followed by dietary provocation is the most important diagnostic tool. Intradermal skin testing, serological and gastroscopic food sensitivity tests are not reliable alternatives for diagnosing AFRs (Kunkle and Horner 1992, Jackson and others 2003, Halliwell and others 2004, Verlinden and others 2006). The home-prepared diet is considered the gold standard elimination diet (Reedy and others 1997, Hill 1999, Scott and others 2001, Biourge and others 2004) but requires a great deal of cooperation from the owner over a period of several weeks (Tapp and others 2002). Lack of owner compliance is one of the main reasons that up to one-third of dogs enrolled in food trials at referral centres do not complete the programme (Chesney 2002, Tapp and others 2002, Loeffler and others 2006).

No age or sex predispositions for AFR have been identified (Carlotti and others 1990, Denis and Paradis 1994, Chesney 2002, Verlinden and others 2006). Although AFRs can occur at any age, initial clinical signs often arise within the first year of life (Verlinden and others 2006). Estimates for average onset age range

from 15 months (Chesney 2002), 2 years (Rosser 1993) and 4 to 6 years (Harvey 1993). Boxers, Cocker and Springer Spaniels, Collies, Dalmatians, West Highland White terriers, Labrador retrievers and German shepherd dogs are reportedly at higher risk for AFR, but these observations have not been confirmed statistically (Rosser 1993, Verlinden and others 2006, Picco and others 2008).

The objectives of this retrospective study were to: (1) determine the prevalence of AFRs in dogs referred to the dermatological clinic of a veterinary teaching hospital; (2) assess breed, sex or age predisposition and (3) test for association between AFRs and selected clinical features.

MATERIALS AND METHODS

The medical records of all dogs admitted to the referral dermatological clinic of the University of Milan from January 2005 to December 2006 were reviewed. Data on signalment, medical and dietary history, physical and dermatological examinations, clinicopathologic abnormalities and diagnosis were retrieved. Cases with incomplete medical records (incomplete recording of clinical features or incomplete follow-up) were excluded.

During the period in question, a standardised diagnostic protocol was followed at the clinic:

1. Ectoparasite infestations were ruled out by clinical examination, coat brushings, hair plucks, skin scrapings and, where appropriate, acaricidal trial therapy.
2. All cutaneous lesion, microbial infections and their distribution were recorded. Microbial skin and ear infections were investigated using acetate tape impression, smears of the external ear canal, cutaneous cytology, dermatophyte culture and/or microbiological culture and treated with topical and/or systemic antibiotics or antifungal therapy as required.
3. Haematological screening for underlying endocrine disorders was carried out where indicated.
4. A skin biopsy was performed on dogs that were not diagnosed with ectoparasitosis, bacterial or fungal disease

and that did not show clinical signs typically related to an allergic disease (see the following text).

Criteria 1 to 4 were used to diagnose non-allergic disease. In the remaining dogs, if clinical signs were still present, the following criteria were used in addition to previous criteria:

5. Strict flea control was applied when there was anamnestic and clinical suspicion of flea allergy dermatitis (FAD). If clinical signs diminished or disappeared after flea control was initiated, FAD was diagnosed.
6. A standardised dietary trial to establish or rule out a diagnosis of AFR was undertaken in the remaining subjects.

The dogs were placed on a restricted home-cooked diet containing a single meat and a single carbohydrate for 8 to 10 weeks. Ingredients were chosen based on information obtained from the owner to ensure that the food had not previously been fed to the patient on a regular basis. At the end of the dietary trial, the dogs resumed their original diet.

The severity of pruritus was assessed by both owners (Table 1) and clinicians

(Table 2), using non-validated pruritus severity rating scales (modified by Crow and others 2001). Skin lesions (papule, erythema, scaling, excoriations and erosions, pyotraumatic dermatitis, pustules and epidermal collarettes, otitis externa, pododermatitis, seborrhoea) and any gastrointestinal signs were also assessed and recorded. Observations were recorded at the initial examination, after 2, 4 and 8 weeks of the restricted diet, at the end of the dietary trial and again 15 days or sooner (depending on recurrence) after dietary re-challenge.

Pruritic co-existing or secondary skin or ear infections were treated with antimicrobials during the dietary trial and challenge if necessary, in accordance with previous studies (Loeffler and others 2006). Oral glucocorticoids were permitted in dogs in which a cycle of inflammation and pruritus had been set up. Glucocorticoids were withheld for at least 4 weeks before the end of the dietary trial, as previously recommended (Loeffler and others 2006, Kotnic 2007).

The diagnosis of AFR was based on criteria reported by Loeffler and others (2006): AFR was diagnosed if pruritus resolved during the dietary trial, but recurred when the dogs were challenged

Table 1. Criteria for evaluation and scoring of pruritus by the owner (modified by Crow and others 2001)

Pruritus category	Pruritus score	Owner observation
Normal	0	Dog not pruritic at all, or scratches occasionally like a normal dog
Minimal	1	Scratching, rubbing, chewing or licking briefly during the day (10 to 30% of day)
Mild	2	Frequent scratching, rubbing or licking during the day (30 to 50% of day)
Moderate	3	Intense scratching, rubbing or licking episodes with signs of distress (50 to 75% of day), but still able to relax and sleep at night
Severe	4	Scratching, rubbing or licking at every opportunity and even at night and during meals, associated with self-trauma

Table 2. Criteria for evaluation and scoring of pruritus by the clinician (modified by Crow and others 2001)

Pruritus category	Pruritus score	Clinician observation
Normal	0	No pruritus (no evidence of self-trauma)
Minimal	1	One to five mild excoriations, involving only one part of the body
Mild	2	Evidence of excoriations on more than one part of the body
Moderate	3	Evidence of pyotraumatic dermatitis or deep ulcerations that are self-inflicted, or scratching, chewing, licking one to five times during the visit
Severe	4	Scratching, chewing, licking constantly, self-mutilation if left unattended

with the original diet. If pruritus did not resolve but was reduced by at least 50% during the trial and subsequently increased by at least one level of score on re-challenge, concurrent AFR was diagnosed and the presence of other pruritic diseases was investigated. If the severity of pruritus decreased during the trial, but did not increase within 2 weeks of re-challenge, it was concluded that the test diet had not influenced the skin disease. Finally, AFR was considered unlikely if pruritus was not reduced during the dietary challenge; atopic dermatitis was diagnosed clinically according to ACVD Task Force on Canine Atopic Dermatitis criteria (DeBoer and Hillier 2001). Any dog that was not correctly maintained on the test diet, did not complete the prescribed therapies or did not complete the trial was recorded as a dropout.

Statistical analysis

Data analysis was carried out using statistical analysis system software (Instat 3.0, GraphPad software, San Diego, CA). Pearson's chi-square test and Fisher's exact test were used to test for associations between breed, sex, age, selected clinical features and AFR. Odds ratio (OR) was used to measure the degree of associations and 95% confidence intervals (CIs) were reported. The Mann-Whitney U test was used to compare the clinician and owner pruritus scores. The level of significance was set at $P<0.05$.

RESULTS

During the study period, 942 dogs were admitted to the veterinary teaching hospital. The medical records of 161 dogs with dermatological signs were reviewed and 31 of these were excluded due to lack of complete data. The records of 130 dogs were included in the study. Sixty-nine (53%) had non-allergic disease and 22 (17%) had only FAD. The remaining 39 dogs (30%) were suspected to have AFR and were subjected to a dietary trial. Six (15%) were excluded from the final evaluation – two refused to eat the test food and four were not fed the test diet exclusively. Of the remaining 33 dogs, the level of pruritus remained unacceptable in 17 throughout

the dietary trial, and atopic disease was suspected. Fifteen of these (88%) were subsequently diagnosed with atopic dermatitis, while two dogs (12%) remained undiagnosed. AFR was diagnosed in the other 16 dogs, accounting for 26% (16 of 61) of dogs with suspected allergic disease. The prevalence for dogs that completed the food trial was 48% (16 of 33), and the adjusted prevalence (Chesney 2002) for those that started the trial was 41% (16 of 39). Prevalence for the entire study population was 12% (16 of 130). Concurrent atopy was diagnosed in 3 of 16 dogs with AFR.

Breed, sex, age and prevalence data are presented in Table 3. Among the dogs with AFR, nine different breeds were represented, including three crossbreed dogs. Prevalence rates for different breed groupings ranged from 0 to 50%; there were no statistically significant associations between breed or age and prevalence of AFRs. The onset age of clinical signs for 10 of 16 (62.5%) dogs with AFRs was less than 1 year (mean 7.3 $\pm$ 3.06 months).

The other six dogs (37.5%) showed signs at 1 to 10 years of age (mean 4.8 $\pm$ 3.06 years). There was a significant association between onset age less than 1 year and prevalence of AFRs (OR=3.8; $P=0.0221$, 95% CI=1.27 to 11.16).

There were no significant differences between owner and clinician pruritus scores. Most dogs had widespread and generalised pruritus (Table 4). Three dogs had atypical caudodorsal pruritus; two of these were diagnosed with concurrent FAD. Perianal pruritus was present in four dogs (25%). Three of these dogs, all German shepherd dogs (19%), had perianal fistulas. One dog with perianal fistulas had pruritus localised only in this region. There was a statistically significant association between perianal fistula and AFR (OR=26.1; $P=0.0058$, 95% CI=2.52 to 269.4). Ten dogs (62.5%) with AFRs had bilateral otitis externa; this was statistically significant (OR=5.9; $P=0.0015$, 95% CI=2 to 17.9). There was no significant association between AFRs and concurrent pyoderma or *Malassezia*

Table 3. Breed, sex and age and prevalence of adverse food reaction (AFR) among 130 dogs with dermatological signs

	Dogs with dermatological signs	Subgroup of dogs with AFR	Prevalence of AFR (%)
All dogs	130	16	12
Breed			
Crossbreed	26	3	12
German shepherd dog	15	3	20
English Bulldog	9	2	22
Labrador retriever	8	0	0
Beagle	6	1	10
Boxer	6	0	0
Maltese	5	1	20
American Staff. Terrier	4	2	50
Other breeds	51	4	8
Sex			
Entire male	63	9	14
Neutered male	7	1	14
Entire female	37	4	11
Neutered female	23	2	9
Onset age (years) of clinical signs			
<1	45	10	22*
1 to 3	40	1	2.5
4 to 10	40	5	12.5
>10	5	0	0
Age (years) at presentation			
<1	18	2	11
1 to 3	33	3	9
3 to 10	66	9	14
>10	13	2	15

*Chi-square analysis indicated a significant difference from total value, $P<0.05$.

Table 4. Comparison of clinical signs and secondary infections at presentation in 130 dogs with dermatological signs, those with adverse food reaction (AFR) and those without AFR. Data are shown as n (%)

Clinical feature	All dogs with dermatological signs (n=130)	Dogs with AFR (n=16)	Dogs without AFR (n=114)
Pruritus	114 (87)	16 (100)	98 (86)
Perianal fistula	4 (3.1)	3* (18.8)*	1 (0.9)
Otitis externa	35 (26.9)	10 (62.5)†	25 (21.9)
Pyoderma	37 (28.5)	7 (43.8)	30 (26.3)
Malassezia dermatitis	22 (16.9)	4 (25)	18 (15.8)
Gastrointestinal signs	3 (2)	1 (6)	2 (1.8)

*Chi-square analysis indicated a significant difference compared with dogs without AFR, $P=0.0058$, 95% CI=2.52 to 269.4.

†Chi-square analysis indicated a significant difference compared with dogs without AFR, $P=0.0015$, 95% CI=2 to 17.9.

‡All dogs were German shepherd dogs.

dermatitis (Table 4). Concurrent gastrointestinal signs were reported in only one dog. These gastrointestinal signs resolved completely during the dietary trial, but recurred together with pruritus after the dog resumed the original diet.

DISCUSSION

In this study population, the prevalence of AFRs among dogs with dermatological signs was 12%. This is higher than previous reports, which estimated that AFRs accounted for 1% (Walton 1967), 1.7 (Wilhelm and Favrot 2005); 3.96 (Denis and Paradis 1994) 5% (Carlotti and others 1990) and 7.6% (Chesney 2002) of all canine skin diseases. In some of these reports, the study population was not clearly defined (Walton 1967, Denis and Paradis 1994, Wilhelm and Favrot 2005). In this study, AFRs accounted for 26% of all allergic dermatoses. Previous estimates were 10 to 15% (Carlotti and others 1990, Scott and others 2001). More recently, AFRs were considered the sole cause of skin disease in 17 to 35% of dogs with non-seasonal pruritus that were submitted to a food trial (Chesney 2002, Biourge and others 2004, Loeffler and others 2006).

The large differences between published prevalence rates are difficult to explain with the limited data available. A systematic review of the literature in 2001 highlighted many difficulties in accurately estimating the prevalence of AFRs: Many of the published reports did not report the population size from which

the dogs were drawn, the number of dogs that were removed from the study, or the criteria used to quantify improvement (Chesney 2001). In most published studies the test population consisted of referred cases with non-seasonal generalised pruritus (Biourge and others 2004, Loeffler and others 2006). The criteria used for selecting the test population will obviously influence the estimated prevalence. Furthermore, the authors of the majority of published case reports on AFRs have focused on clinical signs, diagnosis and treatment, rather than on frequency. Even in human medicine, the prevalence of AFRs is unknown and estimates range between 3 and 34% (Madsen 2005).

If only pruritic dogs subjected to a dietary trial are considered, the adjusted prevalence rate (Chesney 2002) of 41% (16 of 39) in this study was lower than one recent report of 62% (Biourge and others, 2004), but higher than others: 22.4% of 85 referred cases fed a home-cooked test diet (Chesney, 2002); 29.2% of 72 referred cases fed a home-cooked test diet and 32.1% of 109 referred cases fed a commercial test diet (Loeffler and others 2006); and 29.4% of 126 dogs from a non-specified population submitted to an elimination diet (Kotnic 2007). This study supports these recent reports of AFR being involved in over one-third of dogs referred with non-seasonal pruritus, either alone or concurrently with other allergies.

Dropout rates indicate that 15% of dogs with a potential diagnosis of AFR were not properly evaluated, mainly due to lack of owner compliance. This value is lower than previously reported with

home-cooked dietary trials (Chesney 2002, Tapp and others 2002, Loeffler and others 2006). The number of cases lost prior to complete follow-up is frequently not reported in dermatological studies in veterinary medicine (Chesney 2001), but is necessary to more clearly establish the true prevalence of AFR. This observation emphasizes the need for detailed client education and optimal choice of diet until reliable diagnostic alternatives are developed.

Our results regarding a lack of sex predisposition to AFR are in agreement with previous studies (Carlotti and others 1990, Harvey 1993, Rosser 1993). The absence of breed predisposition in this study could be a result of lack of power due to the limited sample size. The high proportion of dogs (62.5%) showing initial signs at a young age confirms that AFR is a disease commonly with an early onset and is in agreement with others (Harvey 1993, Rosser 1993, Denis and Paradis 1994).

Generalised pruritus, often with concurrent bilateral external otitis, was the main clinical sign, and was similar to previous reports (Harvey 1993, Rosser 1993, Denis and Paradis 1994, Verlinden and others 2006, Picco and others 2008). There was a significantly higher incidence of perianal fistula in dogs with AFR in our study, but this data should be interpreted with caution, because all the dogs with perianal fistula were German shepherd dogs; extrapolation to other breeds is not warranted. The results indicate that AFR should be considered as an important differential diagnosis in German shepherd dogs with perianal fistulas. Perineal pruritus was observed in previous studies of AFR, regardless of any association with breed (Rosser 1993, Loeffler and others 2006, Verlinden and others 2006), whereas reports of perianal fistulas in allergic dogs are rare (Haekin and others 1996). In human beings, perianal fistula has been associated with an allergy to cow's milk (Iacono and others 1998). When a group of dogs (mostly German shepherd dogs) suffering from perianal fistulas was exclusively fed a fish and potato diet for an extended period after surgery, there was a lower rate of recurrence with less frequent and severe complications relative to previous studies, in which only surgical

treatment was performed (Lombardi and Marino 2008).

AFRs can cause gastrointestinal and, less frequently, respiratory and neurological clinical signs in dogs (Carlotti and others 1990, Harvey 1993, Rosser 1993, Denis and Paradis 1994, Paterson 1995, Wilhelm and Favrot 2005, Loeffler and others 2006). Gastrointestinal signs were observed in only 6% (1 of 16) of the dogs with AFR; this is similar to previous studies: 2% (Walton 1967), 5.5% (Denis and Paradis 1994) and 9.1% (Carlotti and others 1990). The number of dogs with concurrent AFR and gastrointestinal signs (1 of 16) was small, and did not differ significantly from the proportion of non-AFR cases with gastrointestinal signs (2 of 114). Although these numbers are very small, they illustrate the point that dogs with concurrent pruritus and gastrointestinal disease cannot be presumed to have AFR.

In three dogs with AFR and caudodorsal pruritus, clinical signs resembled FAD rather than AFR. Two of these dogs were diagnosed with concurrent AFR and FAD. Our study revealed three cases with concurrent AFR and atopy, reflecting reported values (Rosser 1993, Denis and Paradis 1994, Paterson 1995, Verlinden and others 2006). In human dermatology, it is now accepted that there are causal links between AFR and atopic dermatitis (Hillier and Griffin 2001, Gustafsson and others 2003). A similar situation may occur in dogs (Jackson and others 2003, Halliwell and others 2004, Olivry and others 2008).

In conclusion, the prevalence of AFRs in our population of dogs was higher than most of the values reported in the literature. Considering the lack of complete data regarding this disease, the authors recommend broader studies to further investigate the true prevalence of AFR, its predisposing factors and clinical markers.

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