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Measurement of allergen-specific IgG in serum is of limited value for the management of dogs diagnosed with cutaneous adverse food reactions

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ABSTRACT

Conflicting results have been reported in the literature in terms of the usefulness of serological testing for IgG against food allergens in dogs with cutaneous adverse food reaction (CAFR). The aim of the present study was to evaluate the suitability of a commercially available IgG ELISA for identifying food allergens in dogs, by challenging dogs with specific food ingredients, selected on the basis of IgG reactivity in serum samples. A total of 24 adult dogs with CAFR were enrolled into the study and 16 healthy dogs were included as a control group. Blood samples were obtained for measurement of specific IgG antibodies against 39 commonly used pet food ingredients by ELISA. Participating owners were surveyed to obtain information on their pet's dietary history. Eleven healthy control dogs and 12 dogs with CAFR were subsequently challenged in a blinded cross-over design experiment with both positive and negative food ingredients, selected on the basis of the ELISA test results.

There was substantial individual variation in ELISA test results to the various food allergens, but no significant difference in IgG reactivity comparing the CAFR and control groups. None of the control dogs developed any clinical signs of an allergic reaction during the dietary challenge study. In the CAFR group, six of 12 dogs developed clinical signs after the negative challenge, and two of nine dogs developed clinical signs after the positive challenge. It was concluded that the ELISA test for dietary allergen-specific IgG is of limited value in the management of dogs with CAFR.

Introduction

An adverse food reaction refers to any clinically abnormal response attributed to the ingestion of a food or food additive (Hillier and Griffin, 2001). Adverse food reactions (AFRs) likely account for 1–6% of companion animal skin disorders seen in first-opinion veterinary practice, and around 10–49% of allergic responses in dogs and cats (Verlinden et al., 2006; Roudebush et al., 2010). However, making a diagnosis of cutaneous adverse food reaction (CAFR) can be challenging, as the clinical signs are frequently indistinguishable from those in other allergic skin diseases, where there is hypersensitivity to other environmental allergens, such as grass pollens or dust mites (Jackson et al., 2005; Picco et al., 2008).

Effective management of CAFR requires allergen avoidance, and therefore discriminating between dietary and environmental causes is crucial and the approach to treatment of CAFR and atopic dermatitis differs markedly (Olivry et al., 2010). The reference standard diagnostic approach for CAFR is based on the performance of an elimination-challenge test, where resolution of clinical signs is expected to occur by feeding a suitable elimination diet for a minimum period of 8 weeks (Olivry et al., 2015), with a subsequent positive response (relapse in clinical signs) following provocation testing, either by feeding a complete diet or multiple/individual dietary ingredients (Olivry and Bizikova, 2010; Hensel et al., 2015). However, this procedure requires a considerable amount of time and effort to identify specific food ingredients as the causative allergens, and owner compliance can be problematic.

Serological testing, for example by enzyme-linked immunosorbent assay (ELISA), is offered commercially to veterinary practitioners to allow them to identify antibody reactivity to individual dietary components. Such tests are designed to measure serum immunoglobulin

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E (IgE) or immunoglobulin G (IgG) against several commonly used food ingredients. However, there are conflicting views as to whether such serology tests are sensitive and specific for identifying dietary allergens and whether they provide useful information that can inform clinical management of CAFR in dogs. Serum IgE testing for dietary allergens is considered to be unreliable as a screening tool for CAFR in humans and numerous animal species (Jeffers et al., 1991; Mueller and Tsohalis, 1998; Guilford et al., 2001; Dupont et al., 2016). Some research studies into canine CAFR suggest that IgG analyses may prove useful in particular circumstances (Halliwell et al., 2004; Bethlehem et al., 2012), while other studies concluded that ELISAs for allergen-specific IgG demonstrate limited value as a diagnostic tool (Hardy et al., 2014; Jeffers et al., 1991; Zimmer et al., 2011).

Previous research studies, designed to investigate serological testing in dogs with CAFR, have not necessarily established whether or not the dietary allergens identified were capable of provoking clinical signs *in vivo*. Therefore, the aim of the present study was to evaluate the usefulness of an IgG ELISA for screening food allergens in dogs, by challenging these dogs with food ingredients, selected on the basis of the presence or absence of serum IgG antibody reactivity.

Materials and methods

Study population

A total of 40 privately owned dogs were recruited into the study (schematic overview of the experimental design and timeline, Appendix: Supplementary Fig. S1>). Dogs with CAFR ($n = 24$) were recruited from the dermatology services of two veterinary referral clinics in the Netherlands. These dogs (Table 1) had been previously diagnosed with CAFR, based on reduction of clinical signs during a dietary elimination trial and recurrence of clinical signs when challenged with the original diet, and their clinical signs were fully controlled with dietary therapy for at least 3 months at the start of the study. Healthy dogs ($n = 16$) were selected from the patient databases of the same veterinary clinics on the basis of being over 1 year of age and having no prior history or clinical signs of skin or gastrointestinal disease.

Blood sampling and IgG analyses

Blood sampling was performed as part of routine veterinary clinical practice, for diagnostic purposes and informed owner consent was obtained for use of residual serum samples for clinical research. Blood was allowed to clot, centrifuged within 20 min of collection and stored at –20 °C until further processing. Serum samples were de-identified and submitted in duplicate to a commercial laboratory in the Netherlands that offers serological screening for food-allergens, using an ELISA as described by Vink (2014) designed to test IgG reactivity against 39 individual dietary ingredients (Table 3). To determine the analytical variation of the commercial assay, the coefficient of variation was determined using the duplicate blood samples ($n = 40$), with an overall CV of <10% being considered satisfactory. IgG values >0.4 U/mL were considered positive, and the recommendation from the laboratory was to exclude any ingredient with IgG reactivity above this value from the diet.

Dietary survey

Owners were surveyed for the purpose of obtaining a dietary history for each dog. The questionnaire collected data on previous and current commercial diets, treats and other sources of food. Owners of the dogs diagnosed with CAFR were also questioned about the composition of any home-cooked elimination diet, the commercial diets that controlled the clinical signs of CAFR in their dogs, and the commercial diets that were suspected or known to provoke clinical signs of CAFR. All owners were asked to also provide specific brand names where applicable.

Food composition by ingredient was determined by consulting the package labels and Internet websites of the specific brands. In case of a closed or inconclusive declaration, manufacturers were contacted to obtain further information on the ingredients used. Dog food manufacturers that were unwilling to provide details of the raw materials used in their diet were asked to provide information on the presence of the 39 allergens in the IgG ELISA panel.

Dietary challenge trial

A total of 12 dogs with CAFR (but free of clinical signs at the start of the trial) and 11 control dogs were included in the dietary challenge study. This was designed as a blinded cross-over experiment to expose dogs to one ingredient (positive challenge), where the serum IgG antibodies were reported to be >10 U/mL and one ingredient (negative challenge), where the IgG antibodies were below the limit of detection. Although the diagnostic laboratory recommended a threshold of 0.4 U/mL for a positive result, we decided to select a potential allergen with a higher value as the positive challenge for the purposes of the study. Although the control dogs

Table 1
Characteristics of the dogs included in the cutaneous adverse food reaction group ($n = 24$).

Dog number	Breed	Sex	Age	Weight (kg)	Age at diagnosis	Clinical signs	Duration of current diet
1	French bulldog	FS	4y 5m	9.8	4y	Erythema, pruritus, otitis externa, interdigital pyoderma	5m
2	Shiba inu × Scottish shepherd	FS	2y 3m	18.0	6m	Cheilitis, pruritus, excessive shedding	1y 6m
3	Beagle	M	7y 5m	16.0	7y	Recurrent malassezia otitis externa, malassezia-paronychia	5m
4	Crossbreed	FS	3y 8m	22.0	3y 4m	Pruritus/erythema abdomen, interdigital pruritus, recurrent otitis externa	4m
5	Spinone Italiano	FS	1y 9m	38.0	6m	Diarrhoea, erythema, pruritus (ears, axillae, inguinal, periocular)	1y 6m
6	American bulldog	M	1y 2m	41.0	11m	Pruritus, papulae on head, dorsum and flanks, periocular swelling, urticae, diarrhea	3m
7	Beagle	M	4y 10m	9.3	4y 3m	Pruritus and brown discoloration tail base	7m
8	Dachshund	FS	5y 2m	9.6	4y 5m	Pruritus, hyperpigmentation, hyperkeratosis (interdigital, axillae, inguinal area)	9m
9	German shepherd	FS	1y 6m	37.8	1y	Pruritus pyoderma (abdomen, dorsum, thorax)	6m
10	German shepherd	FS	2y	36.5	1y 6m	Pruritus axillae inguinal area	6m
11	Rottweiler	FS	2y 11m	47.5	1y	Recurrent otitis externa	1y 10m
12	White shepherd	F	1y 4m	33.5	1y	Diarrhoea, hair loss, pruritus, licking feet	4m
13	Chow chow	FS	4y 1m	20.4	2y	Alopecia/ pruritus dorsum and abdomen	2y 1m
14	Old German shepherd	F	1y 6m	32.6	1y 2m	Otitis, pruritus, pyoderma abdomen	4m
15	French bulldog	M	1y 10m	11.0	1y 6m	Pruritus axillae, ventral thorax	4m
16	Crossbreed	M	7y 5m	10.0	7y	Recurrent pyoderma, otitis externa	5m
17	Polsky owczarek nizinny	M	9y 7m	20.0	9y	Interdigital pruritus, pruritus elbows, groin, otitis externa	7m
18	Soft coated wheaten retriever	M	8y 2m	17.0	7y 9m	Otitis externa, pyoderma, yeast dermatitis inguinal area/abdomen	3m
19	French bulldog	M	2y 6m	9.0	2y	Flank alopecia, scaly dry skin	6m
20	Bullmastiff	M	6y	48.0	4y 6m	Otitis externa, folliculitis, conjunctivitis, interdigital pyoderma	1y 6m
21	Labrador retriever	F	9y 1m	32.5	8y 7m	Interdigital pruritus, pyoderma, otitis externa	4m
22	French bulldog	M	4y	15.2	7m	Demodex, pyoderma, pruritus	3y 6m
23	Bouvier des Flandres	M	1y 6m	45.0	1y 2m	Generalized pruritus	4m
24	Jack Russell terrier	FS	2y 3m	7.2	1y 9m	Interdigital pruritus, otitis externa	6m

F, female; FS, female spayed; M, male; y, year; m, month.

Table 2
Characteristics of the dogs included in the control group ($n = 16$).

Dog	Breed	Sex	Age	Weight (kg)
1	Old English bulldog	M	4y 0m	25.0
2	Old English bulldog	F	4y 0m	35.0
3	Old English bulldog	F	1y 0m	24.0
4	Australian cattle dog	F	5y 11m	21.0
5	Bobtail	MN	6y 3m	26.0
6	Labrador retriever	FS	8y 2m	30.0
7	Spinone	MN	5y 1m	38.8
8	Labrador retriever	F	7y 1m	27.0
9	Labrador retriever	M	4y 1m	28.0
10	Landseer	F	4y 7m	60.0
11	Crossbreed	M	1y 2m	36.5
12	Crossbreed	MN	11y 0m	30.0
13	Welsh Corgi Cardigan	MN	12y 9m	17.0
14	Crossbreed	F	1y 2m	23.0
15	Belgian Malinois	F	1y 1m	26.0
16	Belgian Malinois	F	2y 9m	31.5

F, female; FS, female spayed; M, male; MN, male neutered.

were allocated by convenience sampling to start the trial with a positive or a negative ingredient, we decided to use the negative challenge as the first arm of the cross-over study in the dogs with CAFR, to reduce the chance of dropouts during the first stage of the study period due to clinical relapse. The dog owners and the study dermatologists who monitored the dogs were masked to the sequence of the two challenges. The challenge ingredients were provided in addition to the normal diet the dogs received from their owners at 5 g/kg body weight for a maximum duration of 14 days. If the dog responded by showing cutaneous clinical signs (as determined by the study dermatologists), the challenge was discontinued immediately and the outcome was considered positive. Clinical signs of CAFR were treated according to routine veterinary protocols. If no clinical response was observed during the 14-day challenge, the outcome was considered to be negative. The washout period between the two challenge phases was at least 14 days, or longer for dogs with a positive reaction, such that all dogs that progressed to the second phase were free of cutaneous clinical signs.

Data analysis

Descriptive statistics were used to summarise the data, using Microsoft Excel 2013. IgG values for individual ingredients were compared between control dogs and dogs with CAFR using the independent samples Mann–Whitney *U* test in IBM SPSS statistics, version 21. The level of statistical significance was set at $P < 0.05$.

Results

Study population

Table 1 provides details of the dogs with CAFR enrolled in the study. The mean (±standard deviation) age and weight of the control dogs were 5.0 (±3.5) years and 29.9 (±9.8) kg, and those for the dogs with CAFR were 4.0 (±2.6) years and 24.5 (±13.8) kg. Age and weight were similar between the control and CAFR groups ($P = 0.30$ and $P = 0.18$, respectively). Table 2 provides details of the control dogs that were considered eligible for the study.

Allergen-specific IgG ELISA

IgG reactivity against the different food ingredients did not differ significantly between dogs with CAFR and controls (Table 3). The mean (±standard error, SE) number of food ingredients that showed a positive IgG antibody response in individual dogs (IgG > 0.4 U/mL) was 16 (±1.3) for the dogs with CAFR and 17 (±2.0) for the control dogs, which was not significantly different ($P = 0.59$). The calculated overall CV of the IgG ELISA assay was 2.62%, well within the acceptable limit of 10%. Fig. 1 shows serum IgG values (U/mL) for food ingredients in both groups.

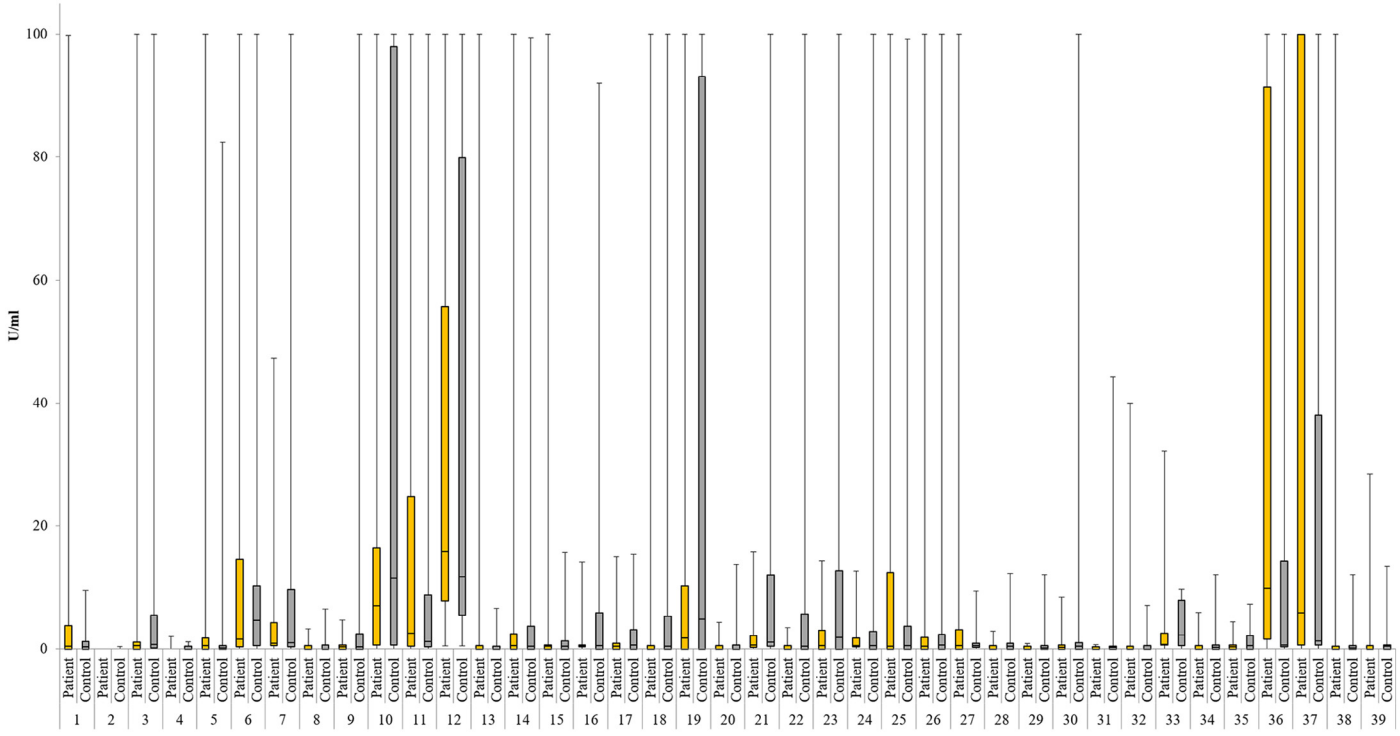

Fig. 1. Box-plot of serum IgG values (U/mL) measured by ELISA against food ingredients for control dogs and those diagnosed with cutaneous adverse food reaction (CAFR). The upper and lower hinges represent the 75th and 25th percentiles of the dataset. The band within the box represents the median. The whiskers illustrate the range of the dataset. Ingredients: 1, European hake; 2, herring; 3, tuna; 4, salmon; 5, veal liver; 6, veal; 7, turkey; 8, chicken; 9, lamb; 10, beef; 11, beef liver; 12, beef tripe; 13, prok; 14, potato; 15, corn; 16, beet root; 17, green beans; 18, sugar beet; 19, tomato; 20, carrots; 21, peas; 22, soy; 23, garlic; 24, watercress; 25, casein; 26, cow milk; 27, flaxseed/oil; 28, barley; 29, oats; 30, wheat, 31, buckwheat; 32, cassava; 33, millet; 34, rice; 35, wild rice; 36, yeast; 37, brewer's yeast; 38 chicken egg yolk; 39, chicken egg white.

Table 3
Median and range of serum IgG values (U/mL) measured by ELISA against food ingredients for control dogs and those diagnosed with cutaneous adverse food reaction (CAFR).

Food ingredient	Controls		CAFR		*P*
	Median	Range	Median	Range	
European hake	0.375	0.00–9.50	0.48	0.00–99.85	0.613
Herring	0.00	0.00–0.40	0.00	0.00–0.00	0.521
Tuna	0.70	0.00–100	0.53	0.00–100	0.389
Salmon	0.00	0.00–1.21	0.00	0.00–2.00	0.404
Veal liver	0.18	0.00–82.38	0.49	0.00–100	0.304
Veal	4.66	0.00–100	1.56	0.00–100	0.713
Turkey	0.99	0.00–47.57	0.93	0.00–47.33	0.652
Chicken	0.00	0.00–6.51	0.00	0.00–3.28	0.452
Lamb	0.38	0.00–100	0.38	0.00–4.64	0.420
Beef	11.46	0.00–100	7.03	0.00–100	0.539
Beef liver	1.19	0.00–100	2.52	0.00–100	0.420
Beef tripe	11.80	0.00–100	15.89	0.00–100	0.633
Pork	0.00	0.00–6.58	0.00	0.00–100	0.733
Potato	0.47	0.00–99.48	0.58	0.00–100	0.795
Corn	0.44	0.00–15.76	0.48	0.00–100	0,967
Beetroot	0.51	0.00–92.04	0.43	0.00–14.12	0.774
Green beans	0.62	0.00–15.40	0.44	0.00–15.10	0.345
Sugar beet	0.44	0.00–100	0.00	0.00–100	0.174
Tomato	4.80	0.00–100	1.81	0.00–100	0.613
Carrots	0.00	0.00–13.74	0.00	0.00–4.33	0.989
Peas	1.13	0.00–100	0.61	0.00–15.82	0.292
Soy	0.49	0.00–100	0.00	0.00–3.43	0.090
Garlic	1.91	0.00–100	0.53	0.00–14.28	0.183
Watercress	0.55	0.00–100	0.56	0.00–12.69	0.946
Casein	0.52	0.00–99.15	0.41	0.00–100	0.733
Cow milk	0.62	0.00–100	0.45	0.00–100	0.774
Flaxseed/oil	0.50	0.00–9.40	0.50	0.00–100	0.967
Barley	0.47	0.00–12.29	0.00	0.00–2.90	0.157
Oats	0.19	0.00–12.14	0.00	0.00–0.84	0.452
Wheat	0.44	0.00–100	0.23	0.00–8.40	0.557
Buckwheat	0.22	0.00–44.31	0.00	0.00–0.65	0.304
Cassava	0.00	0.00–7.10	0.00	0.00–40.00	0.613
Millet	2.27	0.00–9.75	0.70	0.00–32.14	0.613
Rice	0.24	0.00–12.12	0.00	0.00–5.93	0.345
Wild rice	0.49	0.00–7.21	0.37	0.00–4.40	0.436
Yeast	0.66	0.00–100	9.91	0.00–100	0.107
Brewer's yeast	1.33	0.00–100	5.91	0.00–100	0.486
Chicken egg-yolk	0.19	0.00–12.08	0.00	0.00–100	0.420
Chicken egg-white	0.46	0.00–13.48	0.00	0.00–28.50	0.389

Dietary survey

Results from the dietary survey showed that the CAFR group was exposed to significantly fewer food ingredients (mean ± SE, 17.4 ± 1.27) than the control group (6.9 ± 0.88; $P < 0.001$). The type of food ingredients that both groups of dogs were exposed to also differed considerably. The most frequently consumed food ingredients in the control group were chicken, turkey, rice (all 100% exposure), corn (94% exposure) and beef (88% exposure). In the CAFR group, the most frequently fed ingredients were rice and potato (63 and 58% exposure), followed by sugar beet, lamb and flaxseed oil (42, 38 and 33% exposure, respectively). Most of the dogs in both groups had ingested at least one food ingredient in their current diet against which they also showed serum IgG antibody reactivity (Figs. 2A, B). However, all of these dogs were free of clinical signs despite this.

Dietary challenge trial

The results of the dietary challenge trial for the CAFR group are shown in Table 4. None of the dogs in the control group ($n = 11$) demonstrated any adverse clinical signs during the dietary trial. Of the 12 dogs with CAFR that were enrolled into the dietary trial, three dogs did not complete the study, due to development of severe cutaneous clinical signs during the first phase of the cross-over trial. Six dogs with CAFR developed clinical signs after the negative challenge, and two dogs developed clinical signs after the positive challenge. One dog reacted during both the negative and positive challenge phases, and four dogs did not develop any clinical signs during the trial.

Discussion

The present study was performed to evaluate the application of an IgG ELISA panel for screening food allergens in dogs. Based on the research findings, it was concluded that the IgG ELISA used in this study was of limited value in differentiating between CAFR-affected and healthy dogs and was not specific for food allergens that could provoke CAFR. The lack of any clinical signs in healthy dogs, demonstrating serum IgG reactivity to food antigens present in their current diet, suggests that this likely represents a normal component of mucosal immunity, rather than a hypersensitivity reaction that can potentially lead to systemic clinical signs, which is similar to the situation in humans (Stapel et al., 2008). Twenty-two of the 24 dogs with CAFR were reported to be demonstrating significant IgG reactivity to food ingredients in their current diet, despite these dogs being free of clinical signs on their current diet. In contrast, several positive responses were detected in food ingredients which were not reported in the animal's dietary history. This may reflect an immunological response to food items which were consumed earlier in life, or may indicate a lack of specificity of the IgG ELISA.

When comparing the research findings of the present study to those reported in the scientific literature, some similarities and discrepancies can be identified. The results of the present study contradict those reported in a previous publication, evaluating the same commercial test (Vink, 2014). The inclusion of healthy control dogs and the more robust inclusion criteria (based on established challenge protocols and excluding secondary skin manifestations and behavioural problems) in the current study might explain these different outcomes. Bethlehem et al. (2012) recently studied the effectiveness of patch testing and measurement of antigen-specific serum antibodies as diagnostic tools in dogs with suspected AFR. For this purpose, 25 allergic dogs and 11 healthy controls were tested for food-antigen specific IgG. As in the present study, no difference in IgG reactivity between CAFR dogs and healthy controls was observed and it was concluded that a positive reaction on the serum IgG antibody test was not informative, but a negative result might indicate mucosal tolerance to the antigen. The latter conclusion was not substantiated in the present study, since 50% of the dogs showed occurrence of clinical signs after being challenged with a food ingredient reported to be negative in the ELISA.

Halliwell et al. (2004) determined food-antigen specific IgE and IgG in sera from three defined dog populations: healthy dogs, atopic dogs and dogs with AFR. As in the present study, food antigen-specific IgG was measurable against almost all allergens included in the assay in almost all sera, although dogs with AFR showed significantly greater IgG reactivity compared with healthy controls. This is not in agreement with the present study and the study carried out by Bethlehem et al. (2012), in which there was no significant difference in IgG reactivity comparing CAFR-affected and healthy dogs. Halliwell et al. (2004) concluded that measurement of serum IgG to dietary antigens was of limited diagnostic value, a similar view to that reached in the present study.

In the recent study reported by Hardy et al. (2014), the variability in results comparing two commercially available food-specific IgG ELISA tests for dogs in the UK was determined using sera from dogs with CAFR, non-food induced atopic dermatitis, an allergic/inflammatory phenotype, miscellaneous skin diseases and healthy dogs. A lack of agreement between the two assays and the inability of either assay to distinguish between dogs of different disease

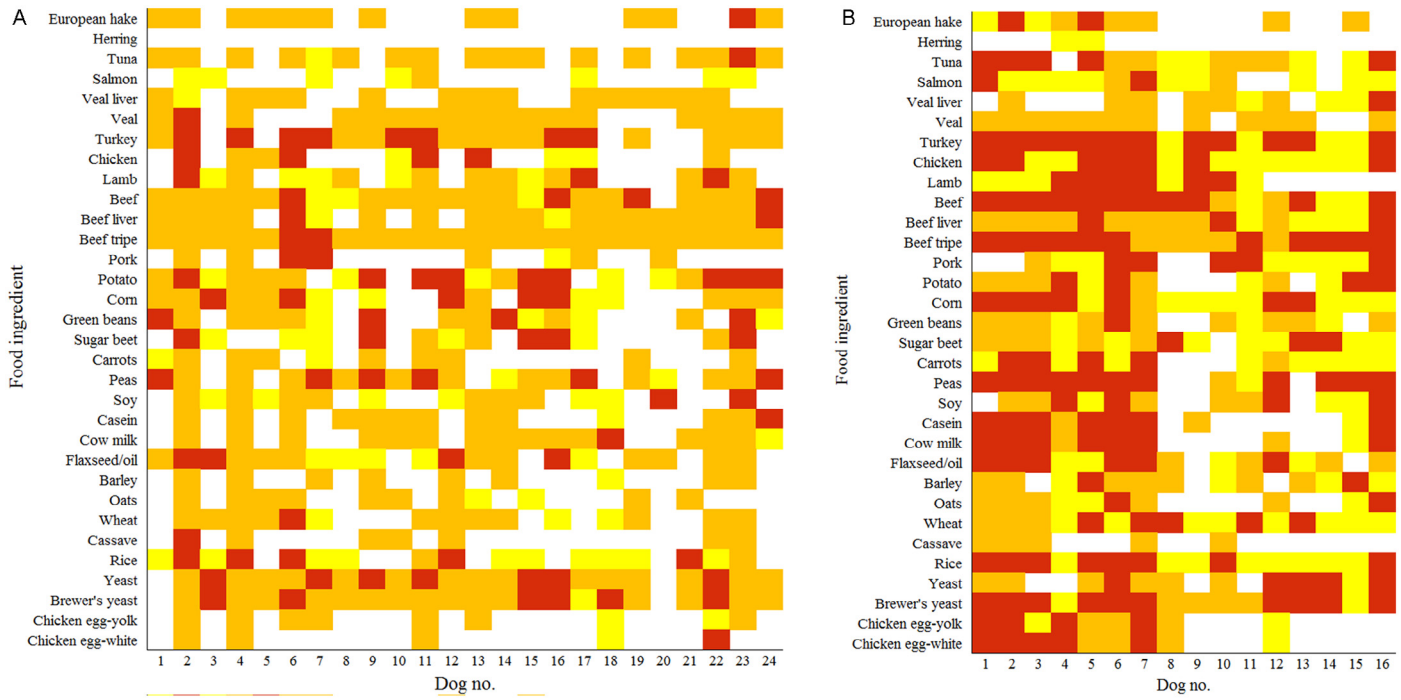

Fig. 2. Food ingredient exposure versus IgG ELISA results in dogs with (A) cutaneous adverse food reactions (CAFR) and (B) healthy control dogs. White: food ingredient not present in current diet, no IgG antibodies present in serum; yellow: food ingredients present in current diet, no IgG antibodies present in serum; orange: food ingredients not present in current diet, IgG antibodies present in serum above the laboratory's positive value (titer > 0.4 U/mL); red: food ingredients present in current diet, IgG antibodies present in the serum above the positive value set by the laboratory.

status led to the conclusion that neither test could be recommended in the clinical management of CAFR.

There are some limitations of this study that merit discussion. The study was based on a relatively small sample of healthy dogs and dogs with CAFR, particularly with respect to the dietary challenge component. Only two food items were selected, based on the ELISA test results, to represent negative and positive challenges. Including more food items might have been more informative in terms of the relationship between serum IgG reactivity and clinical response to challenge. However, this would probably have resulted in fewer participants and lower compliance during extended challenge phases. We attempted to strengthen the study by surveying owners to assess their pet's previous exposure to food ingredients, and comparing results with the presence of IgG antibodies against these items. This method has its limitations, as reliable information of food ingredient intake through a survey can be difficult to obtain (Halliwell et al., 2004). This might also have led to underreporting of dietary ingredient exposure.

Table 4
Ingredients used in the dietary challenge trial and observed responses in dogs diagnosed with cutaneous adverse food reaction (CAFR; $n = 12$).

Dog	Negative challenge ingredient	Positive challenge ingredient	Response to negative challenge	Response to positive challenge
1	Chicken	Yeast	Positive response	No reaction
2	Tuna	Beef tripe	No reaction	Positive response
3	Carrot	Beef tripe	No reaction	No reaction
4	Chicken	Beef tripe	No reaction	No reaction
5	Chicken	Potato	Positive response	Dropout[a]
6	Carrot	Beef tripe	No reaction	No reaction
7	Carrot	Turkey	Positive response	Dropout[a]
8	Chicken	Beef tripe	Positive response	Positive response
9	Potato	Beef tripe	No reaction	No reaction
10	Chicken	Beef liver	Positive response	Dropout[a]
11	Chicken	Beef tripe	Positive response	No reaction
12	Chicken	Turkey	No reaction	No reaction

[a] Dropout indicates that the dog demonstrated a positive response to the negative challenge ingredient and did not progress to the second arm of the dietary trial.

Conclusions

The IgG ELISA used in the present study was of limited value in discriminating between healthy dogs and those with CAFR and in identifying the food allergens responsible for the clinical signs of CAFR. There was a lack of agreement between serum IgG reactivity and previous exposure to dietary ingredients. Positive responses to dietary ingredients that were incorporated into the exclusion diet and used to control the clinical signs of CAFR were reported.

Conflict of interest statement

The research was funded by Utrecht University and Wageningen University. None of the authors have any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.tvjl.2017.01.009.

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