Food Allergy in Dogs and Cats: Current Dermatological Perspectives

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INTRODUCTION

Food intolerances include allergic reactions and non-immunological reactions to food components. Pharmacological reactions to substances such as histamine can cause vasodilation and trigger skin disorders. In humans, the incidence of food allergy is increasing in developed countries, with one third of anaphylactic shock flares attributable to food allergy [1].

Food allergies in humans have been known for nearly a century. In 1923, Dr. Prausnitz injected himself intradermally with serum from a fish-allergic individual (Mr. Küstner), and the allergy was confirmed by a positive skin test with Prausnitz reacting to the intradermal injection of fish extract 24 hours later. This was the first passive transfer test, indicating that a reaginic substance was present in the serum of a food-allergic patient.

In the veterinary literature, hypersensitivity reactions to various foods have been reported in dogs, cats, cattle, pigs, horses, rabbits and even pandas and walruses [1-14]. The first cases of skin disorders in dogs were described in 1934 by Pomeroy (allergy to salmon) [15] and subsequently in dogs and cats in 1967 by Walton [2], who in 1968 also published the case of a milk-allergic cat, confirmed by a positive skin test [16].

Until the end of the last century, 1 to 6% of all dermatological diseases and 5 to 20% of allergic dermatitis were thought to be attributable to food allergy [4-8, 11, 17]. These percentages are variable, possibly because the offending food items had still not been identified and reintroduced [1]. In cats, the prevalence of food allergy with cutaneous manifestation was 21% in a group of 73 cats (15 out of 73 cats) [18]. More recently, some authors have observed that 20 to 35% of cases of non-seasonal canine pruritus were due to a food reaction [19-22]. In a recent study the prevalence of food allergy with dermatological signs was 12 %, 26 % in dogs with allergic skin disease and 48 % of those subjected to dietary trial [18a].

AETIOLOGY AND PATHOGENESIS OF FOOD ALLERGY

The specific immunological mechanisms involved in food allergy are not clearly understood, but type I (immediate anaphylactic response), type II, type III (Arthus) and type IV reactions have been suspected [6, 23]. In humans, type I reactions (IgE-mediated) are predominant [24], and the allergens are generally glycoproteins with a molecular weight between 10 and 60 kilo Daltons [25].

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Atopic children are predisposed to showing signs of food allergies, and in 40% food allergens can trigger attacks [26]. We have observed that food allergy onset rarely occurs concomitantly with other pruriginous dermatitis, particularly atopic dermatitis and flea allergy (or allergy to flea bites) dermatitis, which occurs in around 1% of cases [27]. However, in a more recent study involving 96 atopic dogs (sensitized to environmental allergens), 22 (23%) also turned out to suffer from food allergy [28]. Moreover, around 25% of food-allergic dogs also present with atopic dermatitis [22]. The veterinarian should expect an incomplete response to the elimination diet in such situations involving food allergy.

In contrast to what the majority of dog owners think, the offending antigen is usually a basic food ingredient in the animal's diet, theoretically containing proteins of an unknown nature. Antigen sensitization usually follows a long period of up to two years or longer before clinical manifestations occur [12, 13].

These ingredients include meat (beef, chicken, pork, horse, lamb and fish), eggs, milk, rice, soy, wheat, corn and other cereals. In most cases, the pruritus is due to one or two allergens; some studies have reported that one-third to two-thirds of dogs are intolerant to more than one food, e.g. two or more (actual multi-sensitization being exceptional) [6,10,11,14,17,29-33]. Sequential and multiple challenges should be performed (see diagnosis) [34]. Food allergy may be caused by commercial canned or dry foods, which can contain some of these ingredients [6, 18].

The implication of these ingredients varies according to region. In one review of the literature, Roudebush *et al.* observed that beef, dairy products or wheat represented over 65% of reported allergy cases in dogs, while chicken, eggs, lamb or soy represented 25% cases (10 studies, 253 dogs) [35]. Accordingly, it is likely that corn, pork, rice and fish are rarely implicated.

A study based on 10 dogs with identified food allergy has shown that bovine IgG is a major allergen in cow's milk and that it can be a source of cross-reactivity with beef and probably with lamb because of the high homology with ovine immunoglobulins (similarly as for meat allergy in humans). Also it was shown that phosphoglucomutase is an important allergen involved in allergic reaction to lamb and beef [35a]. Another study showed that bovine serum albumin was an IgE-reactive beef component one dog allergic to beef [35b].

In cats, over 89% of cases reported were due to beef, dairy products or fish (8 studies, 45 cats) [35].

Reactions to seafood and fruit have not been implicated in domestic animals. Although it is theoretically possible, additives or preservatives are not considered to be a cause of food allergy in dogs and cats, unlike in humans, as is the case for sulphites [23]. There are no reports documenting such a reaction in animals [34]. Cooking does not affect allergens in humans [24].

In humans, it is likely that food allergy to poultry meat is a distinct disorder with crossreactivity among chicken, turkey and other poultries (associated food allergy to egg-components being unlikely) [35c]. More generally, cross-reactivities are known in human allergy, e.g. between fishes, shellfishes, cow's and got's milks, and fruits [35d]. Cross-reactions between pollens and

vegetables or fruit, which are numerous in humans [24,35d,36], have not been reported, apart from one specific case involving a Japanese dog sensitized to Japanese cedar pollen. The patient presented with oral symptoms (oral allergy syndrome) including salivation and oedema of the lips and tongue after ingesting tomato but not heated tomato juice [37]. However, August reported frequent cross-reactivity among cereal antigens [5].

Food allergy models have been created in dogs producing elevated IgE levels [38-42]. These dogs or their offspring were sensitized parenteraly to various food allergens and demonstrated dermatological or gastrointestinal signs during oral challenge, as well as elevated specific IgE levels and positive skin tests. A colony of Maltese-beagle dogs spontaneously manifesting signs of food allergy was studied at the University of North Carolina [43, 44]. The dogs showed clinical signs (pruritus, otitis and occasionally gastrointestinal signs) when they were fed with soy, chicken or corn. They came up with elevated food specific IgE levels post challenge. In one study, atopic dogs had elevated food specific IgE levels [45]. Another study based on antigen-specific histamine release suggested that IgE-mediated hypersensitivity against food allergens could be involved in canine food hypersensitivity [45a]. It may be considered that true IgE-mediated food allergies occur as a result of genetic predisposition and gastrointestinal barrier abnormalities [36]. A recent study showed that there were no significant differences in food-specific detectable IgE and IgG antibodies before and after an elimination diet of 6-8 weeks in a group of 19 dogs in which 14 were probably food allergic and 7 were proven food allergic [45b]. A study in 11 food allergic dogs showed that 9 of them had a lymphocyte blastogenic response when exposed to offending food allergens, suggesting that lymphocytes reactive to food allergens may play a role [45c]. A last recent study confirmed that lymphocyte reactions to food allergens might be related to the pathogenesis of food allergy in dogs [45d]. Another recent study indicated that the immunopathogenesis of adverse food reactions is different from that of canine atopic dermatitis, based on the predominance of CD8(+) T cells in the former [45e]. The elimination diet relieved clinical signs but did not influence T cell phenotypes or expression of the cytokine and transcription factor genes in the skin of dogs with adverse food reactions, indicating a continuously pre-activated immune status in dogs sensitised to food constituents.

HISTORY AND CLINICAL ASPECTS

No sex predilection has been observed. The prevalence of food allergies is higher in newborns and young children [26]. It has been observed that the age of food allergy onset can range from a few months to over 10 years of age for both dogs and cats [6, 10-13, 28,32]. It should be emphasised that in some studies, young dogs (aged under one year) were commonly affected, as opposed to the situation for atopic dermatitis [12, 17, 32]. Moreover, unlike atopic dermatitis, no family genetic predilection was recognised in food allergy, although some canine breeds such as Boxers, Dachshunds, Terriers and Labrador retrievers might be predisposed, and Siamese cats may also show a predisposition [11-13, 17, 19, 23].

Non-seasonal pruritus is the most common manifestation of food allergy [1-18, 23, 29-32, 34, 46]. The period between ingestion and the onset of signs may depend on the predominant type of hypersensitivity and the specific antigens involved (see diagnosis), but most dogs and cats presenting with food allergy have permanent pruritus that is not obviously diet-related. It is

usually severe, relatively constant from onset, and oral or parenteral glucocorticoids provide results ranging from poor (particularly in longstanding cases and in cats) [5, 11] to good [12-14], which makes this response a poor diagnostic criterion [34]. In the case of poor pruritus response to glucocorticoids, food-allergic dogs can present with iatrogenic Cushing's syndrome [5].

Some authors report the gastrointestinal signs usually described in humans, such as vomiting and diarrhoea, in only 10 to 15% of cases in cats and dogs [2, 6, 11, 17, 47], while others put this figure at around 30% of cases in cats [10,14,48] (although occasionally these are the only clinical signs apparent for food allergy). Jackson reported observing intermittent vomiting, diarrhoea, signs of colitis or borborygmus in 50 to 60% of canine cases [34]. Loeffler reported that 65% (36) of the 56 food-allergic canine patients presented with gastrointestinal signs (as opposed to 21 out of 85 atopic cases, or 25%), and the elimination diet resulted in their disappearance in two-thirds of cases [22]. In this study, perianal pruritus was also more frequent in food-allergic dogs than in the atopic cases (6 vs. 2). Paterson reported 20 cases of colitis-associated cutaneous food allergy [33]. The colitis associated with perianal fistulas can respond to high-dose prednisone and diet therapy [49]. In a recent study the prevalence of associated gastrointestinal signs was only 6 % [18a]. The association of adverse food reactions with perianal fistulas was also demonstrated in dogs in this recent study [18a].

Neurological signs (convulsions) are rarely observed in dogs [2, 9, 12]. The Loeffler's study reported behavioural changes in 3 dogs [22]. Many owners reported that their dogs appeared to improve after an elimination diet was started [23]. Although food allergy-induced canine asthma is very uncommon, its presence has been mentioned [2].

In dogs, erythema and a papular eruption can occur and represent the most common primary lesions. Other primary cutaneous manifestations, such as urticaria and angioedema, may also occur [1]. However, in most cases, secondary lesions predominate and can present rapidly. These include alopecia, excoriations, crusting, lichenification, hyperpigmentation and hyperhidrosis. Pyotraumatic dermatitis, superficial bacterial pyoderma (folliculitis), *Malassezia* dermatitis, otitis externa (which can be exclusive), bacterial pododermatitis, perianal furunculosis and secondary keratoseborrheic disorders are common complications [6, 9, 11, 12, 17]. It is significant that chronic otitis is observed in 56 to 80% of cases [11, 12, 19, 32]. Pruritus and lesions may be generalised, but as with atopic dermatitis, facial lesions and rubbing of the face, pododermatitis accompanied by biting the extremities, bilateral otitis externa and axillary/inguinal involvement occur frequently [2, 3, 11, 12, 22, 34]. Otitis externa appears to occur with approximately the same frequency as atopic dermatitis (55 to 80% of cases) [22]. This was confirmed in a recent study in which there was a significant association between adverse food reactions and otitis externa in dogs [18a], with 3 times more dogs with otitis in a food allergic canine population than in a non-affected population. Otitis externa (and media) can also occur in man in case of food allergy [34a].

It has been reported for a certain time that food-allergic dogs can present with signs typical of atopic dermatitis [6,32]. Some cases of clinically defined canine atopic dermatitis (CAD) will respond to an elimination diet whereas there are pruritic dermatoses other than CAD (see above) which will do the same.

- According to Loeffler (2006) 40% of adverse food reaction cases have a CAD pattern [22].
- According to Picco (2008), amongst cases of allergic skin disease, 71% are CAD *sensu stricto*, 25% are adverse food reactions and 4% are complex [49a].
- According to Favrot (2010) 23% of CAD cases are food-induced [49b].

Clinicians will say that food allergy can mimic CAD (linked to aeroallergens) or that food allergy can be a cause of CAD. There is obviously a clinical overlap. The International Task Force on Canine Atopic Dermatitis supports the concept that cutaneous adverse food reactions (food allergies) might manifest as atopic dermatitis in some canine patients, or, in other words, that food components might trigger flares of atopic dermatitis in dogs hypersensitive to such allergens [49c]. In other words, CAD being a clinical diagnosis, there are cases of food-induced CAD and cases of non-food-induced CAD, which include CAD *sensu stricto* and atopic-like dermatitis [49b]. In clinical practice every dog diagnosed with nonseasonal (i.e. perennial) atopic dermatitis should undergo one or more dietary restriction-provocation challenges (i.e. "elimination diets") [49c].

One case was reported with clinical signs mimicking flea allergy dermatitis [22]. A few cases of recurrent superficial pyoderma have been attributed to a food reaction, in spite of the absence of pruritus [19, 32]. According to Loeffler, secondary pyoderma and *Malassezia* dermatitis are as common in food allergy as in atopic dermatitis (30 to 55% and 20 to 30%, respectively) [22].

A case of granulomatous sebaceous adenitis and one case of dermatosis mimicking mycosis fungoides resulting from a food allergy have been reported [50, 51]. A case of erythema multiforme was reported in 1999 (beef and soy), and another in 2006 (commercially available foods) [52, 53]. In a prospective study involving 24 dogs with claw disease, Mueller observed a partial remission in 2 patients and complete remission in 2 others after an elimination diet; the complete remission patients relapsed 2 days following reintroduction of their old food. One proved to be allergic to beef by sequential rechallenges, which were not performed in the other 3 dogs. Curiously, in three of these four dogs, apoptosis was not demonstrated on histological examination of the claws. Mueller recommended setting up an elimination diet during claw disease only [54].

Non-seasonal pruritus from food allergy in cats may be generalised or primarily involve the face, head and neck with papules, erythema, excoriations and crusting. Ulcerations have been observed in some severe cases of cervico-facial pruritus. Miliary dermatitis, eosinophilic plaque, ulcer and granuloma, symmetric alopecia, erythemato-ceruminous otitis externa or even urticaria and angioedema may occur [3, 10, 11, 13, 14]. Two cases of generalised non-pruriginous squamous crusting dermatitis related to infiltrative lymphocytic mural folliculitis (with interface dermatitis and apoptotic pan-epidermolysis) were attributed to a reaction to commercial food [55, 55a]. In fact infiltrative lymphocytic mural folliculitis is a common histopathological reaction pattern in cats with allergic skin diseases, including food allergy [55b].

DIAGNOSIS

Diagnosis of food allergy is based on the history and clinical signs as well as implementing a trial diet, which is always justified in case this is suspected (e.g., clinical signs of non-seasonal atopic

dermatitis in dogs) [34, 54]. Complete or partial improvement of pruritus during the elimination diet is the main criterion for suspected food allergy. The diagnosis is confirmed by the recurrence of clinical signs when a food administered previously is reintroduced in the diet.

By definition, a hypoallergenic diet should contain ingredients to which the patient has not had prior exposure. Patients rarely respond to the elimination diet during the first week. Some patients experience a distinct reduction of pruritus during the second or third week of the diet [11]. Therefore, the diet period should be a minimum of three weeks [11, 32]. Usually, a few additional weeks (up to 13 weeks) of hypoallergenic diet may be required for a food allergy diagnosis to be suspected [5-7,9-14,17]. The ideal period appears to be 9 to 10 weeks [12, 13] even if many patients show improvement before this period. No other food is permitted during the trial period. In addition, no supplements, vitamins, treat or even pieces of hide or chew toys are allowed. Even very small quantities of allergens can trigger clinical signs: the Maltese-beagle dogs reacted to soy and pork-flavoured milbemycin tablets. As low a quantity of one gram of corn for a dog weighing 5 kg (or 200 mg/kg) can trigger a reaction [44]. In some cases, if a treatment administered concomitantly with glucocorticoids or antibiotics is required, the diet should be continued for at least 2 weeks after the medical treatment has been discontinued [6,11]. Compliance is not always good, and communication is essential. Up to one-third of prescriptions are not followed, even in referred dogs and with the use of commercially available foods [12, 19, 21,22,56]. This may be due to cost or palatability problems [34]. However, good communication with owners is essential, as demonstrated in one study where the compliance failure rate dropped from 52% to 27% after implementing an approach based on a clear model and diagram-based explanation [19]. In a recent study, the prevalence for dogs that completed the home-cooked diet was only 48 % [18a].

Historically, home-prepared diets were the first to be used and have been the gold standard because they can be prepared while avoiding foods that have already been given [54]. They include meat as a protein source and a vegetable as a carbohydrate source of for dogs, and meat alone for cats. In Europe, an elimination diet usually includes lamb, horsemeat or fish cooked with potatoes, turnips or boiled tomatoes. Perhaps potential cross-reactivity between lamb and beef [35a] or various poultries [35c] has not been enough taken in account, even if no crossed-reaction has been clearly demonstrated [30]. Although the elimination diet may be unsuitable for long-term nutrition, gastrointestinal problems are rare. If constipation or diarrhoea occurs, the respective quantities of meat and vegetables should be varied [11]. In cats, a source of food taurine is necessary for all diets not specifically formulated for cats, but elimination diets do not have to be supplemented with taurine sources because the diet is generally short-term and the taurine content of fresh meat is elevated [46,57]. These diets are difficult to implement with regard to obtaining supplies and preparation and are not suitable for the long term or for growing dogs, particularly the large breeds [31, 54, 58].

Generally, commercial foods for animals contain numerous food components and additives, and switching from one commercial food to another is not recommended [5, 7, 9-11]. However, using foods that contain new ingredients, particularly novel protein sources, may be feasible. Some dogs and cats react well to these diets [14, 59]. Unfortunately, in several studies these foods have shown a lower diagnostic acuity compared to home-prepared diets [30, 56, 60, 61].

In addition, some studies have reported that animals that respond to a home-prepared diet do not tolerate the commercial food equivalent [6, 10, 12, 30]. In particular, White made an interesting observation in dietary trials during which seven dogs experienced an improvement in their state of health by a lamb and rice-based diet, but then relapsed with other food diets. The exacerbation of clinical signs also occurred during a canned lamb and rice-based diet. This might have been caused by the metal of the tin [6]. A similar finding was observed in one dog allergic to egg [30] and 2 dogs allergic to soy [20]. It has been demonstrated that cats can show elevated salivary IgA levels related to the casein of canned foods while this level is zero with regard to untreated casein. Thus, the immunogenicity of certain proteins is increased in canned foods [62]. Finally, two studies report the case of dogs that responded well to a home-prepared diet but which could subsequently not tolerate commercial foods based on novel proteins. In one of the studies, 4 out of 8 dogs that had responded to a home-prepared diet relapsed with a commercially produced food containing fish and potato. In another study, 40 dogs that had responded to a home-prepared diet relapsed with various foods based on novel proteins (chicken and rice, venison and rice, catfish and rice) [56, 61]. A similar study was performed in 20 cats with food allergy confirmed by relapse of symptoms after reintroduction of the previous food. Eight cats (40%) relapsed with a commercial food containing lamb and rice and 13 (65%) with a commercial diet containing chicken and rice (3 cats reacted to both foods) [63]. However, in these studies the food allergen was not identified. Additives could not be implicated (cf. above) [34].

More recently, hydrolysate-based commercial foods have appeared on the market and have been shown to be effective in diagnosing food reactions. The proteins contained in these foods (chicken and chicken liver in Hill's Z/D®, soy in Purina HA® and Royal Canin Hypoallergenic®) are reduced by enzyme action to polypeptides that are theoretically too light to cause an IgE-mediated allergic reaction [64]. This presumes that most of the food reactions that will disappear with these foods are immediate reactions, which has not been demonstrated [34]. It has been shown that the thioredoxin reduction of disulfide bonds significantly mitigates the allergenicity of wheat for highly sensitised laboratory dogs [65]. It is possible that the nature of the protein source and the degree of hydrolysation affect the clinical response to this type of food, as has been proven in experimentally sensitised dogs [66]. Hydrolysation probably does not allow all proteins to be reduced to small polypeptides much lower than 10 kD, and some authors recommend prescribing hydrolysate that does not come from a protein source already ingested by the animal [67]. However, it has been demonstrated that a hydrolysed chicken-based food contained 96.9% of molecules of less than 10 kD, with an antigenic mass of 1.5% compared to the intact protein (using the ELISA-inhibition test) and chicken albumin serum absent from the hydrolysate, which suggests its utility [64]. In an experimental study, soy-sensitized dogs did not respond to oral administration of hydrolysed soy protein, suggesting the usefulness of hydrolysed soy protein in diets formulated for the management of dogs with adverse reactions to food [67a]. A preliminary randomised blinded study involving 10 dogs spontaneously sensitised to soy or corn and fed with a hydrolysed soy and corn starch-based product (Purina HA®) showed an approximately 50% reduction of pruritus in 6 soy-allergic dogs and 80% in 4 corn-allergic dogs [68]. In one study, 11 out of 14 dogs (79%) with spontaneous food allergy, confirmed with soy and corn (the Maltese-beagle dog study), did not react to this same food (3 out of 14 or 21% reacted) [44]. Using as a reference the frequency in one recent study of food allergies diagnosed in dogs with allergic dermatitis (atopic pattern) using a home-prepared diet, or about one-third

(19 out of 58) [19], the results obtained in other studies with hydrolysate-based foods are good using a diet involving chicken hydrolysate (Hill's Z/D®) with 20% (9 out of 46) exclusively and 20% (9 out of 46) in association with atopic dermatitis [21], or soy (Royal Canin Hypoallergenic®) with 31% (18 out of 58) exclusively and 28% (16 out of 58) in association with atopic dermatitis [20]. However, in this last study 2 dogs that did not improve with the hydrolysate responded for one year to a home-prepared diet and one to a rabbit-based commercial food. Recently, a remarkable retrospective study [22] demonstrated that a 6-week diet using a chicken hydrolysate (Hill's Z/D®) had the same diagnostic acuity (15 out of 109 dogs or 18.3%) as a home-prepared elimination diet based on food history (10 out of 72 dogs or 17%); in both cases relapse was triggered by reintroduction of the original food. In addition, 11 dogs presented with partial remission in the home-prepared food group (18.3%) and 20 in the hydrolysate group (24.4%) because of another simultaneous pruriginous dermatosis, mainly atopic dermatitis. In both cases there was no significant difference between the two groups (food allergy alone or associated), which shows that a hydrolysate-based food may be a valid alternative to a home-prepared diet, being as useful as this "gold standard" even if this study only gives an indication of the value of the diets, with variations between the two groups of dogs. It should also be mentioned that the lack of compliance was not lower in the hydrolysate group in this study (24.7% compared to 18.1% in the home-prepared food group; difference not significant). Furthermore a recent study clearly confirmed the value of a hydrolysate in 12 dogs sensitized to chicken [68a]. In this study dogs displayed a severe clinical response when eating whole chicken whereas the clinical score was significantly reduced in 11 of the 12 dogs when fed hydrolysed chicken (with no relationship of IgG and IgE responses with specific dietary exposure). However, a review stated that between 20 and 50 % of dogs ingesting partial hydrolysates derived from food items to which they are spontaneously hypersensitive exhibited increases in clinical signs of food reaction [68b]. Unfortunately this is based on only one published study [44] and 2 abstracts. The authors of this review concluded that hydrolysates containing diets are probably best used in dogs suspected not to be hypersensitive to their individual components. The author of this paper is not convinced by this conclusion based in fact on only one published study [44] and clearly in contradiction with the subsequent study [68a]. Cases not diagnosed by a hydrolysate-based diet are probably very rare, but in the case of uncertainty, the successive use of several diet types may be considered [20]. More recently a novel elimination diet composed of a mixture of amino acids and potatoes was considered as effective as an elimination diet and a provocative challenge lead to the identification of an offending food in 11 out of 15 cases [67b].

To confirm the diagnosis, improvement of cutaneous signs when the patient follows an elimination diet as well as a recrudescence of signs when the patient's initial diet is reintroduced must be demonstrated. Re-challenges can simply confirm the food allergy when the old food is reintroduced globally and causes clinical signs, or can confirm it and identify the specific component triggering the reaction if the multiple foods given previously are sequentially supplied as one every 10 to 15 days to determine if a reaction occurs with one (or several) of them [11,22,30,34]. Indeed intolerance to more than one food can occur (see aetiology and pathogenesis). When a food causes recurrence of clinical signs, the previous allergenic diet is used again for at least 15 days or until the symptoms regress; ideally, a second test with the suspect food can be conducted to confirm the food allergy. Patients with food allergy present with an exacerbation of pruritus a few hours or a few days (2 to 7 most often) after ingestion of

the offending allergen, although this may take 2 weeks [11,22,32,34] or even 18 days in cats [63] and 3 weeks in dogs (2 dogs in one study) [61]. One study showed that this duration varied according to the food concerned (4 days for dairy products and 8 days for cereals) [32]. However, the Maltese-beagle dogs sometimes reacted after 15 minutes [34]. If a commercial food is implicated, it may be impossible to determine the allergenic substance exactly, and the best solution may be to use a home-prepared diet, or even better, another commercial food such as a novel protein or novel hydrolysate [5, 6, 9-11].

Interestingly, one study demonstrated that cats responding to an elimination diet did not always relapse after the previous diet was re-established (16 out of 128 cats or 13%) [18]. This was substantiated in a second study where the allergy was not confirmed by food reintroduction in 7 out of 27 cats (26%) [63]. Evidently, the diagnosis was not certain, which indicates that the food allergy may be overestimated when the pet apparently responds to the elimination diet. This may be on account of an absence of reintroduction of the offending allergen, pure coincidence, a temporary reaction or spontaneous remission [63]. Moreover, some owners may be reluctant to carry out re-challenges. The offending allergen is often identified in dogs, but cat owners, conversely, are often disinclined to allow reintroductions to take place [11]. This may be related to the severity of the symptoms and the spectacular effects of the elimination diet. Although less satisfactory, this is not necessarily to the cats' detriment, given that the ultimate goal is to establish a long-term, well tolerated diet [11].

Theoretically, controlling food allergies can reduce the significance of other allergens (for example, aeroallergens) by allowing dogs to go under a pruritus "threshold"; the animal is then considered as presenting only with a food allergy [6,10,11].

It is apparent that food sensitisation gastroscopic tests do not allow the food allergy to be diagnosed [69-71]. Recently, the lactulose and rhamnose urinary excretion test has been used to evaluate small intestinal permeability in dogs [72]. Although it might be used to demonstrate a reaction to a provocation test, it cannot be used in current practice [1]. Colonoscopic allergen provocation (COLAP) holds promises as a test to confirm the diagnosis of suspect IgE-mediated food allergy in dogs with vomiting, diarrhoea and pruritus [72a]. The practical value of this test in canine dermatology remains to be evaluated.

Skin tests with food extracts have not been conclusive and cannot be used to confirm a food reaction [23, 44, 73-75], even if atopic dogs present with positive skin tests more frequently than healthy dogs [75]. This is probably on account of modifications of the allergen composition caused by its digestion or preparation or incorrect test allergen dilution.

In humans, the importance of serological assays involving anti-food component IgE antibodies, including ELISA and RAST (radioallergosorbent test) is controversial [1, 24]. Although increases in serum IgE concentrations can be measured in individual food-allergic dogs, post challenge or before and after an elimination diet (see aetiology and pathogenesis), these are not statistically significant and cannot be used to predict clinical hypersensitivity [7, 9, 11, 29, 44, 74, 76-78]. The situation is likely to be the same in cats. At best IgE assays for food allergens may orientate the selection of elimination diets. One study could not demonstrate food antigen-

specific IgE antibodies in the serum of food allergic dogs using the PK and oral PK tests [79]. Lymphocyte blastogenic tests are not used in practice.
Very recently, a study not yet published evaluated the interest of patch testing in the evaluation of adverse food reactions in dogs [80]. Reactions with patch testing and increased IgE and IgG concentrations were interpreted as true positive when a rechallenge with the respective protein led to deterioration and subsequent feeding of the elimination diet again led to improvement of clinical signs. Sensitivity of the patch testing was 97 % and specificity 89 %. Measurement of specific IgE revealed a specificity of 92 % and a sensitivity of 81 %. Negative predictability was 99 % for patch testing and 82 % for IG assays. It was concluded that patch testing and food antigen-specific antibodies may be useful in selecting the food sources for the elimination diet due to their high negative predictability.

Skin histopathology is not considered diagnostic but rather as compatible with a food allergy. In dogs, it is usually characterised by various degrees of acanthosis (which can be severe) and spongiosis, and superficial perivascular dermatitis with numerous neutrophils and occasionally eosinophils. However in some cases lymphocytes and histiocytes predominate. Mast cell may be numerous. Perifolliculitis can occur. In cats, acanthosis is variable and often accompanied by ulceration and exudation. Severe epidermal and follicular spongiosis and mucinosis (eosinophilic plaque-like) can occur. Dermal inflammation includes eosinophils, mast cells (which can be numerous), histiocytes, lymphocytes and variable neutrophils (numerous in case of ulceration). Deep eosinophilia (very suggestive of food allergy in head and neck lesions) and flame figures can be associated. Eosinophilic luminal or mural folliculitis are seen. Predominant mononuclear infiltrate or minimal inflammation (in case of symmetrical alopecia) have been reported [9, 11, 81].

Differential diagnosis in dogs includes atopic dermatitis, flea allergy dermatitis, ectoparasitoses (sarcoptic mange, cheyletiellosis), drug reactions, bacterial folliculitis and *Malassezia* dermatitis. Food allergy may be suspected in recurrent cases of superficial bacterial pyoderma and chronic otitis externa. In cats, the differential diagnosis includes flea allergy dermatitis, feline atopic dermatitis, drug reactions, dermatophytosis, cheyletiellosis, notoedric mange, contact dermatitis and idiopathic miliary dermatitis [2-4, 7, 9, 14].

CLINICAL MANAGEMENT

The primary treatment of food allergy involves avoiding the offending food item(s) identified during the elimination diet. A varied, well-tolerated home-prepared diet, sometimes balanced with vitamin, mineral and fatty acid supplements, can therefore be used successfully. As indicated above, home-prepared diets for cats do not have to be supplemented with taurine since the taurine content is elevated in fresh meat [20]. A hypoallergenic prescription diet based on novel proteins or hydrolysate (according to the specific established diagnosis) is preferable since it is more appropriate regarding diet and compliance [5-7,9-11,14,23,34]. A novel diet composed of aminoacids, potato proteins and corn starch did not lead to significant increases in skin lesions or pruritus of ten Maltese-beagle atopic dogs hypersensitive to corn [82]. The same diet seemed subsequently to be useful to identify food allergy in 11 of 15 dogs with pruritus (see above) and could consequently be used for the management of food allergic dogs [67b].

New food sensitisations can occur in food-allergic dogs correctly controlled with an appropriate diet, although this may be rare. White reports a period of 1 to 3 years [9]. The frequency of such a new sensitisation is in fact unknown [34]. Rosser and White have proposed the theory of the "immunological window" which establishes that at a certain age genetic predisposition allows the animal to become multisensitised [23]. In any case, a new, well-conducted elimination diet should enable such cases to be demonstrated [34].

When another pruriginous dermatosis is diagnosed concomitantly, it should also be controlled, e.g. by allergen-specific immunotherapy in the case of atopic dermatitis or by eliminating fleas in the case of flea allergy dermatitis. Similarly, secondary complications that exacerbate pruritus, such as bacterial folliculitis, *Malassezia* dermatitis or seborrhoea, should also be controlled.

As indicated above, treatment by parenteral or oral glucocorticoids at anti-inflammatory doses causes a partial or total reduction of pruritus but is not recommended in the long-term, and prolonged therapy can bring about iatrogenic Cushing's syndrome in dogs [5].

The effect of anti-histamines is not clearly understood in the case of food allergy in dogs and cats [1].

CONCLUSION

Diagnosis (by elimination diet) and long-term management (by avoidance) of food allergy, a relatively frequent cause of non-seasonal pruritus in dogs and cats, can be achieved if the clinician is sufficiently rigorous, even if the pathogenesis of the dermatosis is not completely understood at present.

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