

Food hypersensitivity in the cat

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SUMMARY

The term food hypersensitivity refers to all the clinical manifestations of allergy to ingested allergens (immunological mechanisms), and intolerance (non-immunological mechanisms). Few studies of the immunopathogenesis of feline food allergy have been conducted so most immunological data are extrapolated from the human field. The list of incriminated foods varies according to local feeding habits in countries where the animals live. In cats, the most common food allergens are beef, lamb, milk, fish, tinned food and dried food. Food hypersensitivity often manifests in cats as a pruritic dermatosis of the face and neck, miliary dermatitis, self-induced alopecia and generalised scaling or symmetrical alopecia. In addition to the other clinical presentations, all the entities of the eosinophilic granuloma complex should be considered. The incidence of gastrointestinal involvement is underestimated. Most cases of recurrent lymphoplasmacytic colitis seem to be related to food hypersensitivity. In practice, establishing a definitive diagnosis can be difficult and requires a rigorous approach. An elimination diet of one or more foodstuffs, never previously eaten by the cat, should be fed over six to ten weeks, period considered optimal by most dermatologists.

Introduction

The term food hypersensitivity refers to all the clinical manifestations of allergy to ingested allergens (immunological mechanisms), and intolerance (non-immunological mechanisms). However, in the vast majority of cases, neither identification of the actual allergen responsible nor elucidation of the exact immunological mechanisms involved is possible so it may be wiser to use the term food intolerance [11, 12, 14, 27, 31, 35, 39]. Moreover, certain kinds of clinical problem may be associated with the ingestion of foodstuffs but without any evidence of any causal immunological reaction : food can contain pharmacologically active substances (e.g. histamine which induces vasodilatation) [19]; metabolic reactions due to some kind of enzyme deficiency (e.g. lactase) are common ; and both fungal toxins (in dried, poorly prepared or inadequately preserved food) and plant toxins (e.g. tannins and alkaloids) can elicit non-immunological reactions [11].

The incidence of food intolerance in cats is difficult to establish with any precision because it depends on both the definition of food intolerance and to what extent the possibility of food intolerance is considered in the diagnosis. The reported prevalence of food hypersensitivity varies from 1% to 11% of all feline dermatoses [31,36]. In a recent study [5], 6% of all dermatoses in cats were attributed to food intolerance but this figure cannot be taken as definitive because challenge testing

was not routinely undertaken. Food hypersensitivity represents the third most important cause of feline hypersensitivity [5, 11, 12, 26, 35].

Aetiopathogenesis

Few studies of the immunopathogenesis of feline food allergy have been conducted so most immunological data are extrapolated from the human field.

Food allergens

Any foodstuff is potentially allergenic but, in practice, a finite number of ingredients are involved [2, 5, 10, 17, 27, 36, 38, 39]. The actual list varies according to local feeding habits in countries where the animals live. In cats, the most common food allergens are beef, lamb, milk, fish, tinned food and dried food. Less commonly, chicken, gluten and additives can also induce reactions.

The foodstuffs most likely to be allergenic are those which contain the most protein and those which are most commonly fed. The cat will often have been eating the foodstuff in question for a long time [2, 5, 10, 17, 27, 36, 38, 39] and the more a particular protein has been consumed, the more likely it is to induce hypersensitivity [12, 35]. The exact nature of allergenic proteins in cats has never been studied.

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Fig. 1 Facial pruritus and erythema on the lateral pinnae of a cat with food allergy.



Fig. 2 Same cat as in Figure 1, erythema on the lateral pinnae.

It is likely that many foodstuffs are also responsible for non-immunologically based intolerance. Certain fish contain high levels of histamine, e.g. tuna and any dried or inadequately preserved fish. Shellfish – common allergens in humans – have not often been identified as allergens in cats even though they are a common ingredient in “cat treats”. Nevertheless, prawns may induce non-specific histamine release [11, 19].

Most of the commonly suspected additives are haptens (small molecules which are allergenic only when conjugated with a carrier protein), and hypersensitivity to this type of antigen has never been demonstrated in cats. Many of the additives used in the human food industry, like benzoates and tartrazine, are never used in cat food. However, the use of others is widespread, including sodium bisulphite, monosodium glutamate, azo-dyes, sodium nitrite, spices, sodium alginate, vegetable gums, propylene glycol and ethoxyquin [28].

Storage (forage) mites in commercial, dried cat food could be a major source of oral sensitisation for carnivorous animals [13]. In dogs, allergy to storage mites is common although in cats it has never been possible to demonstrate that the sensitivity is specific to forage mites and not due to cross-reaction with house dust mites or mites present in food.

Immune response

The most common immunological response involved in food

Fig. 3 Same cat as in Figures 1-2, lesions of miliary dermatitis.



allergy is probably a Type I immediate hypersensitivity although Type III (Arthus) reactions and Type IV (delayed) hypersensitivity may also occur [5, 12, 14, 27, 31, 35, 36]. Immediate responses appear within minutes or hours of ingestion of the allergen whereas delayed responses take several hours or days. Defence mechanisms to prevent development of food allergy include the protective gastrointestinal mucosa and immune tolerance maintained by cellular immunity associated with the digestive tract [6, 17, 30]. The mucosal barrier excludes most ingested allergens although it is permeable to peptides and small proteins, especially if there is any kind of inflammation, e.g. due to viral or parasitic infection [8]. Although no exact mechanisms have been demonstrated in cats, it is assumed that local and systemic IgA eliminates potential allergens and that any defect in this defence would predispose an animal to potentially damaging hypersensitivity reactions. Food allergy can develop along with other kinds of allergy, e.g. flea allergy dermatitis, atopic dermatitis, etc. [8,19,20].

Clinical features

Food allergy is a non-seasonal dermatosis with no age, breed or sex predilection. Age of onset varies between 3 months and 11 years with most studies showing a mean age of 4 to 5 years [2, 10, 26, 33, 38]. There is no breed predilection although two different studies have shown a higher incidence in Siamese and

Fig. 4 Facial pruritus, erythema, scaling and crusting in a Persian cat with food allergy.





Fig. 5 Erosions around the skin behind the ears in a cat with food allergy.



Fig. 6 Same cat as in Figure 5, blepharoconjunctivitis.

Burmese cats [12, 32, 35]. It is usually believed that food allergy is more common in cats than in dogs although it is impossible to carry out meaningful epidemiological studies because allergic dermatitis is poorly defined and the means of investigating feline allergies are limited [12]. As it is easier to carry out an elimination diet and control flea allergy dermatitis in the cat than it is to perform intradermal allergy testing, food allergy is usually considered the most likely differential in this species (unlike in the dog) after flea allergy dermatitis [12].

Dermatological signs

Clinical signs are not specific although varying degrees of non-seasonal pruritus (either generalised or localised) have been reported in over 90% of cases [2,10,16,18, 26,38]. Response to glucocorticosteroid therapy was good in almost 50% of cases [10]. In some studies, glucocorticosteroids have been found to be less effective although these were either retrospective studies of chronic cases or studies that involved doses similar to those used in dogs [2, 26, 32, 33, 38, 39].

Food hypersensitivity is characterised by a clinical polymorphism [2, 4, 5, 10-12, 14, 18, 26, 27, 31-33, 35, 38, 39]. It often manifests in cats as a pruritic dermatosis of the face (cheilitis and bilateral blepharitis) and neck with erythema, papules, erosions and crusts (Figs 1-9). Bilateral erythemato-ceruminous

Fig. 7 Severe facial pruritus and very crusty lesions in a Persian cat with food allergy (sardines).



otitis, pododermatitis and perianal inflammation are sometimes observed (Figs 10, 11). Food hypersensitivity can also present as miliary dermatitis (Fig. 12), self-induced alopecia and generalised scaling or symmetrical alopecia (Figs 13,14), each of which carries a detailed differential diagnosis. In addition to the other clinical presentations, all the entities of the eosinophilic granuloma complex should be considered, e.g. indolent lip ulcers (Fig. 15) and eosinophilic plaques, wherever they occur [24]. Urticaria and secondary bacterial or fungal infections (e.g. *Malassezia* dermatitis) seem to be relatively rare in cats [10, 31, 32].

Gastrointestinal signs

The incidence of gastrointestinal involvement, which may or may not be associated with dermatological signs, is underestimated. In a series of 17 cases [10], gastrointestinal involvement (e.g. vomiting and intermittent diarrhoea) was observed in 30% of the animals. Most cases of recurrent lymphoplasmacytic colitis, common in cats, seem to be related to food hypersensitivity in this species [6, 17, 22]. In one case, food hypersensitivity mimicked alimentary lymphoma [37].

Diagnosis

In practice, establishing a definitive diagnosis can be difficult and requires a rigorous approach. The animal's history must

Fig. 8 Same cat as in Figure 7 seen after clipping, showing severe erosive and ulcerative lesions on the face.





Fig. 9 Erosions, excoriations and facial pruritus in a domestic short-haired cat with food allergy (beef).



Fig. 10 Same cat as in Figure 9, erythematous pododermatitis.

be thoroughly reviewed, including the cat's living and eating habits, and the diet itself, especially with respect to protein and carbohydrate sources. The physical examination should be methodical. Food hypersensitivity should always be considered in an animal with a non-parasitic pruritic dermatosis [12, 31, 32].

Differential diagnosis

The differential diagnosis is that of all pruritic dermatoses, including initially the ectoparasitic infestations (e.g. cheyletiellosis, notoedric mange, trombiculiasis and pediculosis), other causes of allergic dermatitis and dermatophytosis [5,12, 27, 31, 32, 33, 35, 39]. Facial involvement requires a more detailed diagnostic approach to rule out auto-immune dermatoses, mural lymphocytic folliculitis and certain viral infections [5,12, 27, 31, 32, 33, 35, 39].

Diagnostic tests

Haematological profiles (differential count, etc.) are worthless; at best they might reveal non-diagnostic eosinophilia. Histopathological examination of skin biopsies does not provide any specific information, but usually reveals perivascular inflammation with varying numbers of eosinophils and mast cells, indicating allergic dermatitis in general [9, 10, 12, 31, 32]. In rare cases, histopathological features include a mural lymphocytic folliculitis [4, 9].

Dietary history

Elimination diets

The next stage is to instigate an elimination diet of one or more foodstuffs which the cat has never previously eaten. Although this sounds simple, in practice it can be fraught with problems. This is partly because commercial cat foods nowadays contain a wide variety of different proteins and partly because owners often find it difficult to make their cat follow a strict diet; prior to settling on a diet, it is crucial to assess the owner's motivation [12].

Before the effects of an elimination diet can be properly evaluated, all secondary and concomitant skin conditions must be controlled, e.g. flea allergy dermatitis and secondary infections (although these are rare in cats).

Certain preliminary guidelines are important: the food must be offered on a plate (avoid plastic or metal), toys should be taken away and, in theory, no treats, vitamins, mineral supplements or drugs should be given during the time of the diet [10,12, 25, 27, 31-33, 35, 39].

Prescribing glucocorticosteroids, antihistamines or cyclosporine A cannot always be avoided. In cases, the special diet can be started immediately but, for proper assessment of its effect, it should be prolonged for at least two weeks following the end of the drug course [12, 31, 32]. If pills must be given with food, all protein sources, including butter, cheese, ice cream, meat and animal treats must be avoided. Honey is preferable [25].

Selecting an elimination diet

Protein

In an elimination diet, protein must be restricted to sources never previously eaten by the animal. Duck, horse, lamb and white fish are often appropriate [12, 14, 27, 29-33, 35, 38, 39]. Hydrolysed proteins are low in molecular weight and allergenicity, highly digestible and can be used whatever their origin. Most hydrolysed diets are poultry- or soya-based [3]. None of the industrial foods on the market has a sufficient amount of hydrolysed proteins to guarantee a complete absence of allergens (on average, molecular weight of 12 kd). In fact, in order to guarantee the absence of allergens, it would be necessary for hydrolysed proteins to contain peptides at a maximum level of 1 to 3 kd. This would lead to the cost of hydrolysis and ultrafiltration becoming excessive. It is reasonable to choose an industrial diet that does not contain any protein sources to which the cat may be sensitive. In general, diets containing hydrolysed proteins are effective and well-tolerated [3, 25].

Home-prepared diets

Home-prepared diets should include just one source of protein and one source of carbohydrate. The choice of foodstuffs should take into account the cat's normal eating habits. The choice of diet needs to be a joint decision, taken with the owner, and the cat's eating habits should not be changed too rapidly [12]. The new diet should therefore be introduced gradually, over the course of 4 to 5 days. It should also be given at the same times and correspond to about the same total amount of food



Fig. 11 Same cat as in Figures 9-10, perianal erythema.



Fig. 12 Severe miliary dermatitis in a domestic short-haired cat with food allergy (beef).

as given previously. It must include a relatively lean protein source (lamb, chicken, turkey, horse, duck, rabbit or game), offered either cooked or raw, together with boiled vegetables (potatoes, tomatoes, lentils, banana, pumpkin, etc.). The advantage of these diets lies with the owner having control over all basic ingredients. For cats used to home-prepared diets, they are often more palatable than commercial dry diets (Tab. 1) [12, 25, 31-32, 39].

Tab. 1 Examples of protein and carbohydrate sources in a home-prepared diet [25].

Protein	Carbohydrate
Horse	Rice
White fish	Maize
Duck	Tapioca (cassava)
Chicken	Potato
Turkey	Lentils
Game	Sweet potato
Lamb	Banana
Rabbit	Pumpkin
Ostrich	

Commercial diets

There are a multitude of commercial diets marketed as *hypoallergenic* or for skin allergies [14, 16, 28-33, 35, 39]. These diets fit into three categories:

- *protein coming mostly from specific sources*. These diets cannot be considered suitable as elimination diets as the protein source is too varied.
- *protein coming entirely from specific sources* (e.g. ostrich, kangaroo, catfish, rabbit and duck). These diets are suitable but may contain hidden traces of food allergens.
- *hydrolysed protein*. These diets are theoretically less likely to be allergenic than non-hydrolysed diets. Hydrolysis reduces protein into small, low molecular weight peptides. Hydrolysed diets are therefore the most practical commercial preparations [3, 25, 35]. Hydrolysis effectively reduces the molecular weight and intrinsic antigenicity of the food and also makes it more digestible. These two factors combine to provide low stimulation to the gastrointestinal immune system [3, 25, 35].

The advantage of commercial diets is their ease of use (Tab. 2). However, this should not lead the owner to underestimate the difficulties of sticking to such a diet. A commercial diet should be fed as strictly as a home-prepared diet in relation to amount and timing of feeding, preventing other foods being eaten, checking for gastrointestinal side-effects and monitoring the animal's weight [25].

Tab. 2 Advantages and disadvantages of home-prepared and commercial diets [25].

Home-prepared	Commercial
Advantages:	Advantages:
Owner becomes involved	Practical
No additives	Well-balanced, highly digestible
Control over protein sources	Low allergenicity / hydrolysed
Diversity of protein sources	Palatability
Efficacy	
Palatability	
Disadvantages:	Disadvantages:
Preparation time consuming	No control over protein sources
Often too rich in protein	Additives
Need to balance the diet for growing cats	Large range of foods
Side-effects	Cost
Palatability	Palatability

Monitoring

The patient must be monitored to ensure good compliance. Potential side-effects such as weight loss / gain and gastrointestinal problems, or practical difficulties such as refusing to eat or behavioural changes can also be spotted. To reduce the likelihood of gastrointestinal problems, the elimination diet should be introduced gradually, over at least 4 days, alongside the familiar diet. If the cat loses weight, the diet must be adjusted (for example, protein intake increased) [12].



Fig. 13 Generalised scaling dermatitis (mural lymphocytic folliculitis) associated with eosinophilic plaques in a domestic short-haired cat with food allergy (beef).

Length of diet

Six to eight weeks is considered optimal by most dermatologists. A response can be observed by the end of the third week (Figs 16, 17) but it may take up to 10 weeks for the diet to have any effect [2, 10, 12, 26, 27, 35, 38, 39].

If no response is observed with a hypoallergenic commercial diet, it does not necessarily mean that the cat does not have any kind of food allergy. In this case, a traditional elimination diet should be instigated [30]. If only a partial response is observed, there may be other, concomitant skin problems (and it should be checked with the owner that the diet was rigorously followed). If no response is seen within 10 weeks, the diagnosis should be reviewed. Feeding a cat commercial food ensures a balanced diet – a recent study on hypoallergenic diets prescribed by American vets revealed that 90% failed to provide the officially recommended daily intakes for adult animals [28].

One study investigated the use of two different brands of hypoallergenic product with non-hydrolysed proteins, sold in cans (chicken/rice) and in containers (lamb/rice) for cats with food allergy [16]. Of 20 cats included in the study, 8 experienced relapses with the lamb/rice diet (40%) and 13 cats had relapses with the chicken/rice diet (65%). On the other hand, only 3 of the cats experienced relapses while exposed to the two diets at the same time (15%). Home-prepared diets seem superior to commercial wet food diets, deemed hypoallergenic through diagnostic tests [16].

Fig. 15 Indolent ulcer on the upper lip of a domestic short-haired cat with food allergy (milk).

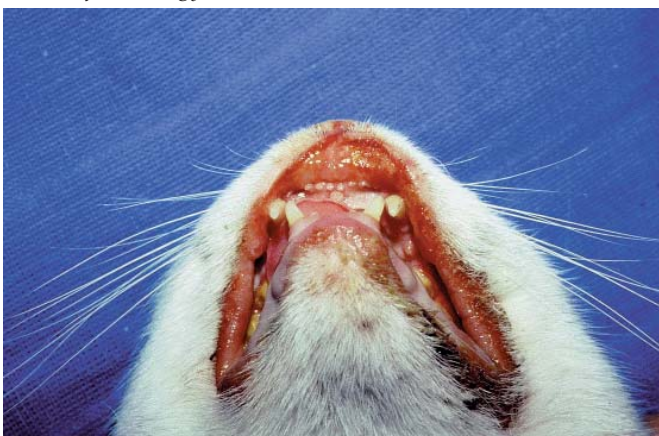


Fig. 14 Self-induced alopecia on the abdomen of a domestic short-haired cat with food allergy.

Challenge tests

The principle of the challenge test is to reintroduce, at regular intervals, each of the foodstuffs for a period of one week and monitor for reappearance of signs. This is a demanding process which is often rejected by the owner, does not absolutely prove that any particular foodstuff is responsible, and gives no information on mechanisms. However, this approach can be useful because few allergens tend to be involved; just one or two account for over 90% of cases [2, 10, 27, 38, 39]. The vast majority of cats do not relapse when an incriminated foodstuff is reintroduced. This may be due to a change in the immune response with time or, more likely, because eating very digestible food for a while gives the intestine time to re-establish normal permeability.

Allergy tests

Allergenic extracts derived from food allergens

Commercially available extracts of animal-derived food allergens (e.g. beef, milk, fish and eggs) are of very variable allergenicity but give satisfactory results in humans. In contrast, studies in humans have shown that extracts of plant-derived food allergens need to be native and prepared immediately before use; laboratory preparations are inactive [30]. However, it has never been possible to extrapolate these findings to cats. There are no published data on what concentrations of these extracts should be used in cats.

Fig. 16 Same cat as in Figure 15, erosions and ulcerations on upper and lower lips.





Fig. 17 Same cat as in Figures 15-16, 3 weeks after starting an elimination diet.

Diagnostic value of intradermal testing and *in vitro* IgE testing

Intradermal skin testing [1, 15], *in vitro* IgE testing [21] and cellular testing have no value in the diagnosis of food allergy in cats. A particular foodstuff cannot be excluded on the basis of a negative result and asymptomatic sensitisation is common [11]. These tests are theoretically useful in human medicine because they are helpful in establishing a more acceptable elimination diet, i.e. a more varied diet can be prescribed once certain important potential food allergens have been eliminated. Even so, opinions are divided on this approach which could get it seriously wrong [7]. It has been stated that "an elimination diet should always be well-constructed and never put together on the basis of a few misleading positive *in vitro* test results".

In veterinary medicine, such an approach is definitely worthless because we can impose as strict a diet as necessary for a period of weeks without any serious problem. Nevertheless, this has not stopped certain companies from promoting food allergen-specific IgE assays to diagnose food allergy. This commercially-appealing approach often goes down well with owners. Whatever the outcome, the change in diet is often associated with clinical improvement, if only because the new diet is more balanced or more digestible than the former one. In this way, food intolerance can be misdiagnosed as food allergy [12].

Treatment

Hypoallergenic diets

The only acceptable, effective way of treating food intolerance is by eliminating the foodstuff(s) responsible. However, this must not adversely affect the nutritional balance of the diet.

Hypoallergenic diets cannot be prolonged for more than 3 weeks without risking skeletal damage [29], unless vitamin and mineral supplements are included. Therefore, owners can either feed their animals a balanced home-prepared diet based on the hypoallergenic diet used in the diagnosis, or give very digestible commercial products [16,25].

Symptomatic therapy

Corticosteroids (1-2 mg/kg prednisolone SID, orally, 0.2 to 0.5

mg/kg dexamethasone BID) are effective especially in the early stages [12, 31, 32]. Antihistamines are ineffective. Some reports have recommended chlorpheniramine (4-8 mg/animal BID, orally) [12, 32]. Cyclosporine A (5 mg/kg SID) can be also used for controlling pruritus and cutaneous lesions associated with food allergy [23, 34].

Treating secondary infections

Secondary skin infections are rare but, in cats with gastrointestinal signs, it is important to control bacteria in the small intestine by prescribing a suitable antibiotic (e.g. metronidazole). The aim of this is to break the vicious cycle of sensitisation followed by the aggravation of gastrointestinal lesions leading to exacerbated dermatological signs [11].

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