

# Cutaneous adverse food reactions in dogs

**Cutaneous adverse food reactions account for between 10% and 25% of dogs with allergic skin disease. A successful elimination diet trial is the key to diagnosing these cases, writes Kathryn Cuddy MVB CertAVP(VD) MRCVS, Skinvet Ireland**

Adverse food reactions (AFRs) can occur at any age, with the most common reactions involving the skin and the gastrointestinal tract. Symptoms are clinically indistinguishable from atopic dermatitis, and definitive diagnosis requires an elimination diet trial and provocative exposure testing. Commercially-available serum tests for food-specific IgE and IgG are not recommended for the diagnosis of AFRs. Excellent client communication is the key to achieving a successful elimination diet trial.

## INTRODUCTION

AFRs are defined as reactions to an otherwise harmless dietary component, which are experienced by certain individuals upon ingestion. AFRs encompass both immunological (true food hypersensitivity) and non-immunological (food intolerance) reactions, with the former being immunoglobulin (Ig)- or cell-mediated.

## CASE STUDY

This series of images documents an elimination diet trial performed on a five-year-old male neutered Shih Tzu, which presented with a history of chronic non-seasonal pruritus. Clinical signs included erythema of the ventral neck (see Figure 4), inguinal region (see Figure 1) and concave ear pinnae (see Figure 2), which resolved after eight weeks on an elimination diet trial (see Figure 3). Several days after a dietary challenge with chicken, he developed periocular dermatitis, which resolved after withdrawal of chicken, thus confirming the diagnosis of an AFR to chicken.

## PATHOGENESIS OF CUTANEOUS AFRS

The pathogenesis of food allergy in humans is well established – it may be IgE-mediated, combined IgE- and cell-mediated, and cell-mediated; it is differentiated from metabolic or pharmacological food reactions. In animals,



Figure 1: Erythema of the inguinal region.



Figure 2: Erythema of the concave ear pinna.



**Figure 3: Resolution of erythema post-elimination diet trial.**

adverse food reaction, which includes immunological and non-immunological causes, is the more appropriate term, as the pathogenesis has not been established.

The immunological mechanisms involved in cutaneous AFRs are complex and poorly understood. The mucosa of the gastrointestinal (GI) tract is confronted with a large variety of foreign antigens, and there are mechanisms preventing exposure of potential food allergens to the immune system, including:

- Breakdown of large, potentially allergenic protein molecules by gastric acids, pancreatic enzymes and intestinal cell lysozymes.
- Movement of food through the GIT by peristalsis.
- The mechanical barrier provided by tight junctions between enterocytes and the mucous layer lining the intestinal epithelial cells.
- Binding of allergenic molecules by secretory IgA in the mucous layer and lamina propria of the gastrointestinal tract.

The immune system of the intestine has to meet the task of discriminating between pathogens and harmless antigens, such as food proteins and commensal bacteria, and to respond accordingly. Despite the large extent of food-antigen exposure, only a small percentage of individuals experience adverse immunologic reactions to food. This is because the normal immune response to dietary proteins is associated with the induction of oral tolerance, which can be considered the default immune response to dietary antigens.

In order for food allergens to be presented to the immune system and generate an inappropriate immunological response, it is likely that there has to be a combination of events involving damage to the protective mechanisms within the GIT along with concurrent ingestion of allergens. The following are situations in which it is speculated that this



**Figure 4: Erythema of the ventral neck.**

set of circumstances may arise:

- It has been demonstrated that infants and very young animals tend to absorb many more peptides and glycoproteins in comparison to adults and the feeding of a wide variety of different foodstuffs at this stage may overload the mechanisms which result in antigenic tolerance.
- It is possible that viral GIT infections and endoparasite infestation may damage the gut wall and contribute to the absorption of antigenic material.
- The presence of a heavy endoparasite burden has been shown to encourage the formation of IgE antibodies, although it is also considered that an endoparasite burden may reduce the likelihood of developing hypersensitivity responses in some individuals.
- There is likely to be a genetic component involved in the development of hypersensitivity responses to food allergens.

	<b>Home-cooked limited-ingredient diet</b>	<b>Commercial limited-ingredient diet</b>	<b>Hydrolysed diet</b>
<b>Description</b>	<b>A home-cooked diet that contains a suitable novel protein and carbohydrate source</b>	<b>A commercially available diet that contains a suitable novel protein and carbohydrate source</b>	<b>The proteins and, in some cases, carbohydrates in these foods have been hydrolysed into small fragments of amino acids and oligopeptides rendering them, in theory, non-immunogenic</b>
<b>Advantages</b>	<ul style="list-style-type: none"> <li>• <b>Gold standard option</b></li> <li>• <b>Contains no additives</b></li> <li>• <b>Not contaminated with other protein or carbohydrate sources</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Straightforward and convenient</b></li> <li>• <b>Nutritionally balanced</b></li> <li>• <b>Suitable for most animals and for long-term feeding</b></li> <li>• <b>Moderate cost</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Straightforward and convenient</b></li> <li>• <b>Nutritionally balanced</b></li> <li>• <b>Suitable for most animals and for long-term feeding</b></li> <li>• <b>Useful where novel proteins cannot be identified</b></li> </ul>
<b>Disadvantages</b>	<ul style="list-style-type: none"> <li>• <b>Time-consuming for owner</b></li> <li>• <b>Cost may be high</b></li> <li>• <b>Animal may refuse to return to commercial food</b></li> <li>• <b>May not be nutritionally balanced</b></li> <li>• <b>May not be suitable for long-term feeding</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Labelling is confusing for owners</b></li> <li>• <b>Up to 80% contain undeclared proteins</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Ingredients and degree of hydrolysis may not be suitable for all animals</b></li> <li>• <b>High cost</b></li> <li>• <b>May see GI upset and weight gain</b></li> <li>• <b>May be unpalatable</b></li> </ul>

**Table 1: Dietary options for elimination diet trial.**

**CLINICAL DISEASE IN DOGS**

The prevalence of cutaneous AFRs in dogs with allergic skin disease is between 10% and 25%, as investigated in a recent literature review.

There is no breed predilection, but since AFRs are commonly reported in individuals with atopic predilection, certain breeds have been reported to be overrepresented. The condition may be seen at any age, although many cases occur in dogs younger than one year of age, and cutaneous AFR is much more common than atopic dermatitis in dogs six months of age or younger. Dogs that develop a pruritic skin disease at an older age (greater than seven years of age), without a previous history of atopic disease, should be carefully screened for adverse food reactions. There is no sex predilection.

There are no pathognomonic clinical signs, and AFR is clinically indistinguishable from canine atopic dermatitis. The most common reactions to ingested food components in the dog involve the skin and the gastrointestinal tract. Skin lesions are classically characterised by non-seasonal pruritus which typically involves the face, feet, ears, axillae, forelegs and perianal region. The pruritus can vary greatly, and the distribution of lesions and pruritus may range from only otitis to a generalised distribution. Secondary infection is common. Less typical presentations include recurrent folliculitis without pruritus, Malassezia dermatitis, seborrhoea, acral lick granulomas, and pyotraumatic dermatitis.

In a published case series, the ear region was involved in 80% of the cases of cutaneous AFR; paws in 61%; inguinal region in 53%; and axillary, anterior foreleg, and periorbital regions in 31% to 37% of cases. However, otitis externa with erythema of the pinnae and vertical canal with minimal horizontal canal involvement was the only cutaneous manifestation of cutaneous AFR in 24% of dogs. Otitis externa may even occur unilaterally only.

Concurrent gastrointestinal disturbances have been reported in 10% to 15% of dogs with cutaneous AFR. Clinical signs include vomiting, diarrhoea, increased number of bowel movements, flatulence, faecal mucous and blood,

and tenesmus.

Food proteins may cause or induce flares of atopic dermatitis and other atopic dermatitis-unrelated conditions, such as urticarial, angioedema, anaphylaxis and gastrointestinal disturbances.

A poor response to glucocorticoid treatment has been reported in the literature, and was statistically significant in the largest study.

**COMMON FOOD ALLERGEN SOURCES**

A 2016 review of all available evidence showed that beef, dairy products, chicken, wheat and lamb are the most common allergens causing cutaneous AFRs in dogs. Beef, fish and chicken are the most common allergens causing cutaneous AFRs in cats. These foods should be the first used for dietary challenge for cutaneous AFR diagnosis. In the limited number of studies which have investigated CAFRs in dogs, most have demonstrated that dogs tend to react to more than one food.

**DIAGNOSIS OF AFRS**

The differential diagnosis of canine AFR is lengthy and includes atopic dermatitis, drug reactions, contact allergy, flea-bite hypersensitivity, pediculosis, intestinal parasite hypersensitivity, sarcoptic mange, Malassezia dermatitis, seborrheic skin disease, and bacterial folliculitis.

**ELIMINATION DIET WITH SUBSEQUENT DIET CHALLENGE**

The diagnosis of AFRs is based on clinical improvement during an elimination diet trial, followed by relapse during a challenge with the previous or suspected diet. This remains the gold standard for the diagnosis of AFR because other tests lack sensitivity and/or specificity.

**LABORATORY TESTING**

A 2017 review of all available evidence evaluated serum tests for food-specific IgE and IgG, intradermal testing with food antigens, lymphocyte proliferation tests, faecal food-specific IgE, patch, gastroscopic, and colonoscopic testing.

They concluded that patch testing with food ingredients might be useful in some selected dogs to choose the ingredients for an elimination diet, and that all other tests cannot be recommended for the clinical diagnosis of AFRs in dogs and cats.

Thus, despite the widespread availability of serum tests for food-specific IgE and IgG, these cannot be recommended for the diagnosis of an AFR.

### WESTERN BLOT

A western blot technique is also available that detects the presence of IgE antibodies in the dog's sera to food extracts from various veterinary prescribed diets and the animal's existing diet. In a recent study, this test performed better than some previously evaluated ELISA-based tests; it was considered potentially useful for identifying appropriate foods for elimination diet trials, but cannot be recommended for the diagnosis of an AFR.

### THE ELIMINATION DIET TRIAL

#### SUCCESSFUL DIET TRIALS

The success of any diet trial relies predominantly on client compliance; the key elements to achieving good compliance are communication, contact and support. It is essential to spend time with the owner explaining the purpose of the trial, the prevalence of AFRs, and how to conduct the trial. Written instructions, advice leaflets, and regular contact throughout the trial will greatly increase the likelihood of the trial being performed correctly.

#### DIETARY HISTORY

A comprehensive dietary history must be established in order to select a suitable diet. This includes details of the main diet, treats, table scraps, fluid intake, food from friends/neighbours/dog walkers, and flavoured medications. It may be difficult to get a complete dietary history in many cases.

#### DIETARY SELECTION

There are three dietary options for performing an elimination diet trial (see Table 1). Proteins and carbohydrates to which the animal has been exposed should be avoided where possible.

#### DURATION OF THE TRIAL

The recommendation for the 'ideal' duration of an elimination diet trial has varied from three to 12 weeks in the past. A 2015 review of all available evidence concluded that the elimination diet trial should last eight weeks in both dogs and cats.

In this review, of 209 dogs with confirmed AFR:

- 50% had achieved a marked reduction of their signs after three weeks;
- 85% were normal after five weeks;
- 95% were normal after eight weeks;
- <5% of dogs needed an elimination diet of up to 13 weeks for a complete remission of signs

and of 40 cats with confirmed AFR:

- 50% were normal after four weeks;
- 80% were normal after six weeks; and
- 90% were normal after eight weeks.

### CONTROLLING PRURITUS DURING THE DIET TRIAL

It is often necessary to control pruritus during the diet trial. This may be achieved with the use of oclacitinib, lokivetmab, or glucocorticoids. Medications should be withdrawn for two weeks prior to final clinical assessment of the response to the diet trial.

### DIET CHALLENGE

If the clinical signs have resolved or improved, or no relapses have been observed, it is imperative to challenge the dog with the original diet to confirm the AFR. The challenge is necessary to prove that any improvement was due to the diet; many cases may improve as a result of other treatments, fatty acids in diets, resolution of infections, flea control, or change of season for dogs that have atopic dermatitis.

The challenge can be done by feeding everything the dog received before the exclusion diet was introduced, or by sequentially adding individual protein and carbohydrate sources to identify individual allergens. Most dogs will relapse within one or two days, but some may take up to ten days. A new food or group of foods should be introduced once every two weeks, while using the diet used for the food trial as the main diet. If worsening of signs occurs, the challenge should be immediately discontinued until signs are once again resolved.

### CLINICAL MANAGEMENT OF AFRS IN DOGS

The prognosis for AFRs is good once offending allergens are identified. The dog should be fed a complete and balanced, highly digestible, limited antigen diet that does not contain the offending ingredients, as identified in the dietary challenges. Management consists of avoiding offending foods, and the prompt addressing of clinical signs when relapses occur through the use of anti-pruritic agents and antimicrobials if required.

### REFERENCES ON REQUEST