Hill’s European Symposium on Advances in Feline Medicine

Brussels, 26th–28th April 2006
Our knowledge of feline allergic skin disease is rudimentary compared to what is known in the dog. In 2001, a Task Force comprising a number of Diplomates from the American College of Veterinary Dermatology reviewed the literature on canine atopic dermatitis and put together a document comprising 24 review papers. Such an endeavour would currently be impossible in the cat owing to the scarcity of publications on the subject.

The major categories of allergic skin disease that have been described in the cat are:
- Flea allergy dermatitis,
- Atopic dermatitis,
- Cutaneous adverse food reactions (food allergies).

**Clinical Appearance of Feline Allergic Skin Disease**

Cats with allergic skin disease have a wider variety of clinical presentations than dogs. This clinical variability has led to the concept of feline cutaneous reaction patterns. Four main patterns are currently recognised:
- Miliary dermatitis,
- Feline symmetrical alopecia,
- Eosinophilic granuloma complex,
- Head and neck pruritus.

These cutaneous reaction patterns are not specific for individual diseases, but are a common reaction of feline skin to a diverse range of diseases including:
- Allergic skin disease (the most important group) – fleas, atopic disease, food allergy,
- Ectoparasite infestation – lice, Otodectes cynotis, Cheyletiella spp., Trombicula spp and Demodex spp.,
- Bacterial and fungal infections,
- Idiopathic,
- Behavioural factors may be present in some cases.
Miliary dermatitis (papulocrustous dermatitis)
This is characterised by miliary, papulocrustous lesions; miliary dermatitis is most commonly located over the dorsum (FIGURE 1), but lesions can be anywhere. It is frequently associated with secondary alopecia, and is most often caused by flea bite hypersensitivity.

Feline symmetrical alopecia
Feline symmetrical alopecia is a bilateral symmetrical alopecia with non-inflamed skin (FIGURE 2). The remaining hair is usually stubby. In most cats it affects the ventral abdomen, caudal hindlimbs and lateral abdomen. The dorsum is not usually affected. Psychogenic forms have been described in nervous breeds, but the most important causes are fleas and other hypersensitivities. It is critical, when presented with this condition, to ascertain whether the cat is licking the hair out, or whether it is falling out. Many owners will think the hair is falling out, while in fact in the vast majority of cases, it is being licked out. If there is any doubt, perform a trichogram (examine some plucked hairs under the microscope).

Eosinophilic granuloma complex
This complex comprises three conditions: the indolent ulcer, eosinophilic plaque and eosinophilic granuloma. They may occur separately or in any combination with each other. The aetiology of the eosinophilic granuloma complex is multifactorial, but hypersensitivity reactions to fleas, food and environmental allergens (atopic disease) appear to be the most significant contributors. The conditions are quite distinctive but cytology can be used to confirm the clinical diagnosis.

Indolent ulcer
Indolent ulcers are well demarcated, alopecic, reddish-brown ulcers with raised borders (FIGURE 3). They usually occur on the upper lips either unilaterally or bilaterally. Pruritus is not commonly observed.

Eosinophilic plaque
This syndrome is characterised by the presence of well demarcated, alopecic, raised plaques with a moist, red surface which may be eroded or ulcerated (FIGURE 4). They are usually located on the ventral abdomen, thorax and medial aspect of the hind legs, but may occur anywhere. These plaques are extremely pruritic and a circulating eosinophilia is often present. Cytology of impression smears reveals large numbers of eosinophils.

Eosinophilic (linear) granuloma
Eosinophilic granulomas are well-defined, firm, raised, yellow to pink lesions (FIGURE 5) that usually occur on the caudal aspect of the hind limbs or in the oral cavity but may occur elsewhere. Oral lesions may cause drooling and dysphagia. They are usually pruritic although this may not always be observed. A circulating eosinophilia is occasionally present and there may be local lymphadenopathy.

Head and neck pruritus
Head and neck pruritus is characterised by severe scratching around the head and neck (FIGURE 6). In most cases alopecia and excoriations are seen and
sometimes ulceration. There are often severe lesions on the cheeks. It has been suggested that pruritus restricted to the back of the neck may also be the consequence of herpes virus infection of nerve endings following vaccination.

Some cats are presented with a combination of two or more of the above patterns at the same time. Other cats show obvious pruritus but without falling into one of the above categories. Despite this, the differential diagnoses remain the same.

**DIAGNOSIS AND MANAGEMENT**

**Flea allergy dermatitis**

Flea allergy dermatitis has been well characterised and usually poses no diagnostic or therapeutic difficulties. Even if direct evidence of fleas cannot be found, modern flea control products are so effective that they can be used for therapeutic trials. In this situation, the treatment is being used for diagnosis and therapy.

**Feline atopic dermatitis**

In the Task Force document, canine atopic dermatitis was defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features, associated most commonly with IgE antibodies to environmental allergens. This definition is important because it encompasses most of the parameters that are used for diagnosis and management of this condition in dogs. For example:

- **Genetic predisposition** accounts for the historical features of early age of onset and predisposed breeds.
- **Inflammatory and pruritic allergic skin disease with characteristic clinical features** accounts for the distinctive clinical phenotype (lesion types and distribution) seen on physical examination that is a major component of the diagnosis.
- **The association with IgE antibodies to environmental allergens** forms the basis of intradermal allergy testing and IgE serology. These tests can be used to support a diagnosis of IgE mediated atopic dermatitis and allow formulation of immunotherapy vaccines.

What evidence is there for the existence of a similar feline disease, and could such a definition be applied to the cat?

**Genetic predisposition**

Apart from one publication that described a pruritic skin disease in three littermates that responded to allergen-specific immunotherapy, there is no convincing evidence for a genetic predisposition to atopic disease in the cat. No breeds of cat are predisposed to the disease and no lines of atopic cats have been described to date.

**Inflammatory and pruritic allergic skin disease with characteristic clinical features**

Unlike the dog, there is, as yet, no defined phenotype for what an atopic cat should look like. Without a characteristic clinical appearance, it is difficult to establish any useful clinical criteria that might point to a diagnosis of feline atopic dermatitis. Cats with presumed atopic disease can present with any of the four cutaneous reaction patterns. To date, there is no evidence that one pattern is more likely to represent atopic disease than any other.
Role of IgE antibodies and environmental allergens

The development of IgE antibodies to environmental allergens is regarded as a pivotal mechanism in the pathogenesis of atopic dermatitis in dogs. Numerous studies have demonstrated that allergen specific IgE concentrations are elevated in atopic dogs with house dust mites being the most commonly implicated allergens. Evidence that cats have a reaginic antibody (IgE) was first reported in cats with Otodectes cynotis infestation.26 Subsequently, DeBoer provided three lines of evidence that feline IgE existed.4 First, a molecule from feline serum was detected on gel electrophoresis that had the same molecular weight profile as canine IgE. This molecule could be removed from feline serum by passing it through a column to which an anti-canine IgE reagent had been attached. Secondly, the anti-canine IgE reagent was able to cause mast cell degranulation in an in vitro feline bladder contraction model of allergic reactions. Thirdly, anti-canine IgE reagents were able to induce wheal formation when injected into cat skin (reverse cutaneous anaphylaxis). More recent studies have used molecular techniques to demonstrate that cats have an immunoglobulin molecule with similar identity to canine IgE.43 Taken together, these studies provide strong evidence that feline IgE exists. Attempts to measure the levels of feline IgE in serum have required the production of reagents able to detect feline IgE directly. This has been achieved in three ways, namely polyclonal antibodies, monoclonal antibodies and the human FcεR1 receptor that is used to measure IgE levels in dogs and humans.44 Unfortunately, studies using these reagents in cats have shown no difference in concentrations of house dust mite specific IgE in cats without skin disease and cats with presumed atopic skin disease. Hence, although feline IgE exists, there is currently no evidence that it is involved in the skin diseases that we currently label as feline atopic dermatitis.

Diagnosis

As a result of the difficulties in establishing precise historical, clinical and immunological features of feline atopic dermatitis, the diagnosis remains a challenge. Histopathology does not provide further specific information that differentiates the various allergic diseases. Biopsies from cases of putative feline atopic disease were shown to contain CD4+ lymphocytes and mast cells in non-inflamed areas, whereas eosinophils are more prominent in lesional skin and eosinophilic granuloma lesions.5,23,34 However, these features would not distinguish between flea allergy, food intolerance or atopic dermatitis. Essentially, the condition should be regarded as a diagnosis of exclusion, once the role of parasites (especially fleas) and food intolerance have been ruled out. Despite the uncertainty surrounding the role of IgE in feline atopic disease, dermatologists still frequently measure levels of mast cell bound IgE by intradermal testing or serum levels by serology once the ‘clinical’ diagnosis has been established by rule-out. Intradermal testing is often unrewarding in cats and far more difficult to interpret than in dogs. The formation of erythematous wheals, even at the positive control site, is much less common than in dogs, although obvious positive reactions are sometimes obtained. Some dermatologists inject fluorescein prior to performing the test to allow reactions to be seen under UV light. This procedure is supposed to improve the visibility of feline reactions although no evidence for this has been advanced to the literature. Although positive reactions are commonly obtained using IgE serology, their precise significance is not known as highlighted above.

Management

Paradoxically, the use of allergen-specific immunotherapy based on intradermal or serological allergy tests can be successful in ameliorating the symptoms of feline atopic skin disease, although reports in the literature relate to open and poorly controlled studies.10,28 A rush protocol has recently been described in a pilot study.42 The mode of action of such therapy in cats is not known and it...
isn’t even clear if it is acting in an allergen specific way or not. Hence, at this stage, it would still be fair to say that the efficacy of this treatment in cats hasn’t been proven.

In many cats, anti-inflammatory medication is required to control the signs of presumed atopic disease. Glucocorticoids are usually well tolerated and still represent the symptomatic treatment of choice.\textsuperscript{12,27,37} Antihistamines have been reported to be effective in a number of cats with atopic dermatitis.\textsuperscript{20,37} Chlorpheniramine is most commonly used although the author has had some success with cetirizine in lesions of the eosinophilic granuloma complex.

The use of cyclosporine is the most recent development in the management of canine and feline atopic dermatitis.\textsuperscript{2,7,9,17,23-25,31,38-40} No controlled studies have yet been published evaluating the efficacy of this drug in cats, but initial anecdotal reports appear promising. The recrudescence of latent toxoplasmosis is a current concern\textsuperscript{1,15} although the true risk of this scenario and its relative risk compared to the use of glucocorticoids have not been established.

Food allergy (cutaneous adverse food reaction)

There are currently no specific dermatological features that distinguish an atopic cat from a cat suffering from adverse food reactions. All four of the cutaneous reaction patterns may be observed. The presence of predominantly facial lesions has often been considered suggestive of dietary allergy and the presence of concurrent gastrointestinal signs can be a diagnostic clue.\textsuperscript{18,28,44} Fish, lamb and dairy products have commonly been incriminated in cases of feline food intolerance.

Pathogenesis

No immunological studies have been reported that elucidate any of the mechanisms that might be involved in cutaneous food allergies in cats.

Diagnosis

There are many pitfalls when undertaking diet trials in dogs and cats. These have been extensively reviewed\textsuperscript{63} and will not be repeated here. In the past, most dermatologists recommended home cooked diets to investigate potential food intolerances.\textsuperscript{33} However, more recently, especially with the introduction of hydrolysed diets, food trials using commercial diets have become more popular. The successful use of such diets has recently been reported in dogs.\textsuperscript{14} The major advantages of commercial diets are that they are nutritionally balanced and improve owner compliance. The length of required diet trials is still controversial. In a study reporting food intolerance in 13 cats, Rosser indicated that up to 10 weeks may be necessary before clinical signs abate.\textsuperscript{41} This finding has not been corroborated in other studies and it is still not known if this is a repeatable result. The principle of the dietary investigation has always been to feed an elimination diet to see if the animal improves, and then to challenge the diet to see if the condition relapses. In the reported literature, this would be considered diagnostic for food allergies. The author adopts a more rigorous approach which requires the above cycle to be repeated, and then to either identify specific ingredients that can trigger a reaction, or to achieve long term control of the condition with diet alone. Owing to these more stringent criteria, food intolerance is a rare diagnosis in the author’s clinic.

Management

The only effective way of managing genuine cases of food intolerance is to avoid the foodstuffs that are involved. Long-term feeding of commercially available limited ingredient or hydrolysed diets are the most appropriate options. Glucocorticoids may have to be used in some cases if dietary manipulation is not possible. Such therapy may also be required if a cat suffers from combination allergy.
REFERENCES

23. Olivry T, Mueller RS. The International Task Force on Canine Atopic Dermatitis. Evidence-based veterinary dermatology: a systematic review of


