FELINE ATOPIC DERMATITIS DEMYSTIFIED

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The atopic cat can be frustrating to diagnose and treat, but in this paper Jennifer Schissler demystifies some of the issues surrounding the condition.

KEY POINTS

1. Atopic dermatitis is a diagnosis of exclusion in cats, and a stepwise approach is essential to reach an accurate diagnosis.
2. Pruritic behavior may or may not be apparent, but recognition of characteristic lesions can help direct the clinician towards the appropriate diagnostic steps.
3. Pruritus relief with consideration for acute and chronic treatment phases is essential; aim to minimize or eliminate glucocorticoids in the chronic phase.
4. Client communication is paramount for success, and owners must be aware that atopic dermatitis is managed lifelong and not cured.

Introduction

Feline atopic dermatitis is an inflammatory, almost invariably pruritic condition with characteristic clinical presentations. Compared to canine atopy, the clinical presentation can be quite different, and less is known about the etiopathogenesis, although – as with dogs – it is a hypersensitivity reaction to certain environmental allergens including pollen, house dust mite and mold. Unlike atopic dermatitis in people and dogs, it is unclear if IgE plays an essential role in the pathogenesis of the condition in the cat, therefore recent publications have advocated for and used the phrase "feline non-flea, non-food hypersensitivity dermatitis" (1). The nomenclature used to describe feline cutaneous allergy is evolving and is not universally accepted; commonly used historic terms include "feline atopy", "feline atopic syndrome", "feline atopic-like dermatitis", and "feline atopic dermatitis". For the sake of consistency, the latter term is used in this article, given its general historical familiarity to readers, and because this condition is the practical clinical counterpart of canine atopic dermatitis.

Diagnosis

Atopic dermatitis is a diagnosis of exclusion. Cutaneous adverse food reactions and flea bite hypersensitivity present with identical clinical signs and may be comorbid with feline atopic dermatitis. Additionally, secondary *Staphylococcus* and *Malassezia* infections can increase dermatitis and pruritus severity. Consideration for and exclusion of infections and infestations, as well as an elimination diet trial in non-seasonal presentations, will prevent unnecessary chronic immunomodulation. A stepwise approach is therefore essential for an accurate and efficient diagnosis, and the following points should be considered in a patient with clinical signs and a history consistent with feline atopic dermatitis:

1. Assess for and treat any known or suspected infestations, and ensure compliance with flea control recommendations.
2. Assess for and treat infections, and assure cytologic resolution of infection.
3. Conduct an elimination diet trial if the patient has non-seasonal signs.

Feline atopic dermatitis will not respond completely to these measures. Although histopathology of feline cutaneous hypersensitivities does not discriminate between flea bite hypersensitivity, cutaneous adverse food reaction or atopic dermatitis, biopsies can support the diagnosis of hypersensitivity in ambiguous presentations. Consider referral of patients with equivocal or incompatible historical features, clinical findings, or lack of therapeutic response to a veterinary dermatologist.

Note that anti-pruritic medications during treatment trials will enhance patient quality of life and owner compliance, but strategic discontinuation of anti-pruritic medication is necessary to assess for response to diagnostic trials.

Clinical signs and diagnosis

Feline atopy manifests a diverse array of characteristic lesions, body distributions, and differential diagnoses. These presentations may occur in isolation or in combination. Some cats present for aggressive hair pulling, scratching and excoriations, whilst pruritic behaviors in other cases may occur in secret, with the patient presenting for progressive, grossly non-inflammatory, symmetric alopecia.

There are four recognized feline cutaneous hypersensitivity clinical patterns: eosinophilic granuloma complex lesions, miliary dermatitis, head and neck excoriation, and symmetric alopecia.

Eosinophilic granuloma complex

Lesions include indolent ulcer (rodent ulcer), eosinophilic plaque, and eosinophilic granuloma (linear or collagenolytic granulomas). Indolent ulcers present unilaterally or bilaterally on the upper lip as eroded plaques **(Figure 1)** and can progress, distorting the upper lip via overall surface ablation and dermal expansion. Eosinophilic plaques present as multiple or singular raised, well-circumscribed erythematous and moist erosions, and are commonly located on the abdomen **(Figure 2)**. Eosinophilic granulomas are typically singular, erythematous, alopecic plaques or nodules often presenting on the inguinal region and hindlimbs, although they may also develop on the chin **(Figure 3)**, tongue, palate **(Figure 4)**, and (rarely) the footpads **(Figure 5)**. Differential diagnoses for these lesions include neoplasia, lymphocytosis, herpesviral dermatitis, and deep fungal or bacterial infections. Eosinophilic granuloma complex lesions are often diagnosed via clinical appearance and supportive history; histopathology may confirm the diagnosis. Note that surface cytology of these lesions typically yields suppurative or pyogranulomatous inflammation with cocci; eosinophils are less numerous and not uniformly found. Treatment of lesions secondarily infected with *Staphylococci* with amoxicillin/clavulanate can result in significant clinical improvement, supporting the theory that bacteria play a role in the development, progression, and perpetuation of the lesions (2). In the author's experience, albeit helpful in many instances, antimicrobials are not always essential for the

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Figure 1. A cat with an indolent ulcer in partial remission; erosions remain on the upper left lip and tissue loss of the upper lip is permanent.

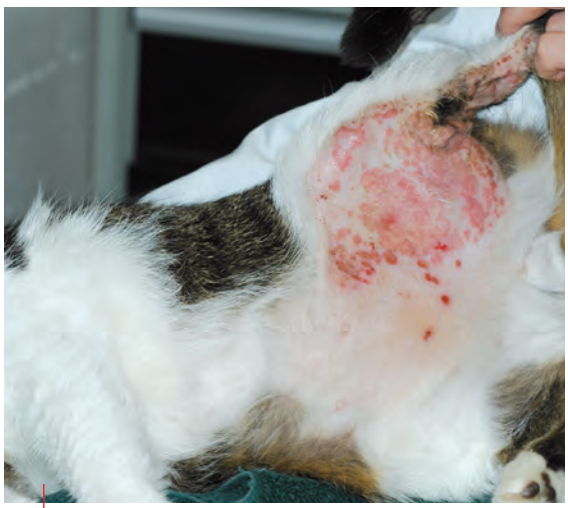

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Figure 2. Multifocal moist, erythematous plaques on the inguinal area and inner thigh.

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Figure 3. An eosinophilic (collagenolytic) granuloma at the mucocutaneous junction of the lower lip.

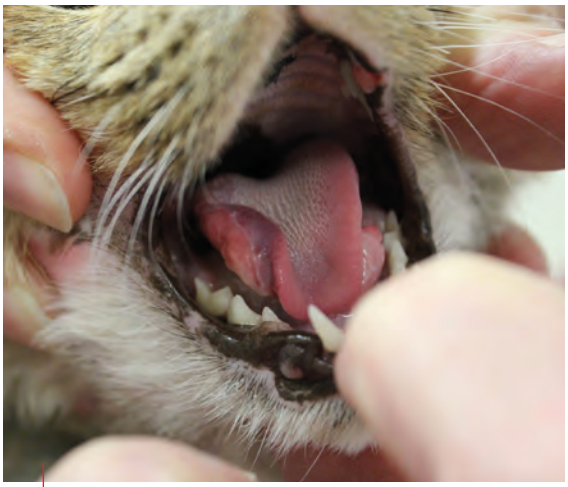

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Figure 4. A granuloma on the lateral aspect of the tongue in a patient with concurrent pruritus and miliary dermatitis. Hypersalivation may develop secondary to the lingual lesion.

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Figure 6. Facial miliary dermatitis with diffuse alopecia.

resolution of eosinophilic granuloma complex lesions, and the decision to use such therapy is based upon cytologic evaluation (see below).

Miliary dermatitis

This is a papular, crusting dermatitis, often distributed on the dorsum, and may present alongside alopecia **(Figure 6)**. Differential diagnoses include dermatophytosis, *Cheyletiella, Demodex cati, D. gatoi,* staphylococcal pyoderma, and pemphigus foliaceus. The diagnostic approach includes cytology from beneath crusts, deep and superficial skin scrapes, and assessment for dermatophytosis, which may include a trichogram, and if negative, PCR and/or culture. Nasal bridge and pinnal involvement may indicate mosquito bite hypersensitivity in outdoor cats. Miliary dermatitis resulting from cutaneous hypersensitivity alone can demonstrate mixed or suppurative inflammation on impression smears of avulsed crusts; eosinophils are variably present, and typically in lesser numbers. Many patients with cutaneous hypersensitivity have secondary staphylococcal pyoderma, which presents as miliary dermatitis. Follow up cytology and clinical examination of patients treated for staphylococcal pyoderma is recommended to discriminate between miliary dermatitis due to allergy, superficial staphylococcal pyoderma, or both in concert.

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Figure 5. An eosinophilic granuloma on the footpad, confirmed via histopathology as neoplasia was a possible differential diagnosis **(a)**. The lesion post-biopsy following two weeks of prednisolone therapy **(b)**.

Head and neck excoriation

This can range from mild to severe, focal to generalized erosions, ulcerations, and alopecia. Hemorrhagic or suppurative exudate and crusts are common, and may occur in conjunction with facial miliary dermatitis **(Figure 7)**. Differential diagnoses include *Notoedres cati* (geographically variable), *Otodectes cynotis*, dermatophytosis, *Demodex* spp., and herpesviral dermatitis. These cases require superficial and deep skin scrapes, and cutaneous cytologic examination for secondary *Staphylococcus* and *Malassezia.* Given that otitis externa may be a manifestation of allergy in cats, scratching around the head and neck necessitates otoscopic assessment, ear cytology and mite preparation. A rare differential is idiopathic ulcerative dermatosis; this manifests as a large patch of excoriation, ulceration and fibrosis at the base of the neck. It is diagnosed via presentation and practical exclusion of hypersensitivity, including lack of response to ectoparasite control, antimicrobial therapy for secondary infection, elimination diet trial, and anti-pruritic therapies. When in question, biopsy can support the diagnosis of hypersensitivity.

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Figure 7. A patient with neck and facial pruritus, erythema, excoriation and miliary dermatitis.

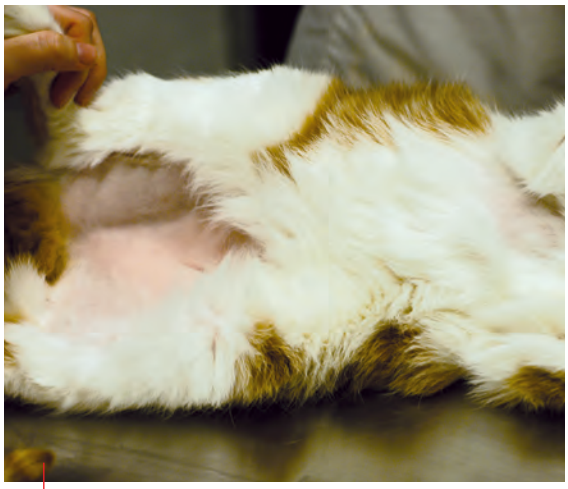

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Figure 8. Bilaterally symmetric, well circumscribed, grossly non-inflammatory alopecia due to barbering in a pruritic atopic dermatitis patient.

Symmetrical truncal and limb alopecia

With its given truncal distribution and gross lack of inflammation, this resembles endocrine alopecia **(Figure 8)**. The hair loss is a result of pruritic behaviors (licking, biting, or pulling of the hair), and is far more common than feline endocrine alopecia. The alopecia ranges in severity from patchy and partial to complete and well-circumscribed, typically distributed over the lateral trunk, ventrum, and distal limbs. Frayed, broken hair tips are apparent upon microscopic examination. In the absence of any other lesions, the primary differential is *D. gatoi,* and if geographically appropriate, the cat fur mite *Lynxacarus radovskyi* (3), so perform superficial skin scrapes. *D. gatoi* is inconsistently found, even with appropriate sampling, but may be identified via fecal flotation due to ingestion during grooming (4). If *D. gatoi* is suspected despite negative scrapes and fecal tests, trial therapy is required. Weekly lime sulfur dips are effective (5), but when to undertake the trial (*i.e.*, early in the diagnostic process, or reserved for patients with presumed atopic dermatitis failing anti-inflammatory therapy) will vary based on perceived geographic prevalence of the parasite, and a history consistent with risk for contagion (*e.g.*, multicat household or shelter). There is mounting evidence for the efficacy of isoxazoline ectoparasiticides (sarolaner, fluralaner) for *D. gatoi* (6) and compelling evidence for this class of drug in treating *D. canis* and *D. injai.* Exclusion of both *D. gatoi* and flea bite hypersensitivity may therefore be performed more conveniently and efficiently with isoxazoline treatment.

Psychogenic alopecia is a differential for barbering cats, and is apparently less common than dermatitis (7). The diagnosis is reached via a lack of response to *D. gatoi* therapy, flea control, elimination diet trial and immunomodulatory therapy [particularly glucocorticoids (7)], in addition to historical evidence consistent with anxiety, and indications of suboptimal living conditions such as lack of environmental enrichment (8). Negative biopsy results with regard to hypersensitivity and response to psychotropic medication and/or environmental modification are additionally supportive. Also uncommon (but worth noting), cats may barber in response to pain due to cystitis, inflammatory bowel disease, or peripheral neuropathy, so if the cause of barbering remains elusive reconsider another thorough physical exam, history, and further diagnostic assessment.

Differential diagnosis

The history and signalment is helpful: patients typically demonstrate clinical signs prior to 4 years of age, and there is no sex predisposition and no well-documented breed predilection. Signs may be seasonal or non-seasonal, and may initially be mild and intermittent, becoming more severe and continuous over time. Both indoor and outdoor cats are affected, with no published assessment of indoor lifestyle as a risk or protective influence. A pruritus score should be obtained (and updated at every recheck), taking care to describe pruritic behaviors: licking, biting, chewing, rubbing, hair pulling and scratching, and identifying the location(s) of the pruritus. The following historical questions can be helpful;

1. At what age did the pruritus start?
2. Is the pruritus seasonal? Atopic dermatitis can be seasonal or non-seasonal.
3. Did the itch start suddenly, or has it become worse over time? In most instances there is increased severity over time.
4. Do other animals in the house have an itch or dermatitis? If so consider ectoparasites (*e.g.*, fleas, *D. gatoi*) or *Microsporum canis*.
5. Has the itch responded to previous treatments? Response to therapy does not make a diagnosis, nor does it discriminate between flea bite hypersensitivity, cutaneous adverse food reaction, or atopic dermatitis, but many hypersensitive cats respond to systemic glucocorticoids.

6. What ectoparasiticides have been given and at what frequency?
7. What is the current diet, and has the cat been fed a different diet previously? This is helpful information for elimination diet trial selection.

Intradermal and serum allergy testing for atopic dermatitis or cutaneous adverse food reaction as a primary diagnostic tool for feline atopic dermatitis is not recommended, as both false positive and negative tests occur. The best use of these tests is when selecting allergens to be included in allergen-specific immunotherapy for atopic dermatitis patients. Note that canine allergen salivary tests, some of which are marketed directly to owners, have shown a shocking lack of accuracy, both with regard to condition (demonstrating positive results in healthy animals) and history (demonstrating positive results to food allergens that the pet has not consumed) (9).

Atopic therapy

A foundation of maintenance anti-inflammatory medication and/or immunotherapy is optimal for chronic management. However, compliance is essential for optimal control of feline atopic dermatitis; educate owners about the chronic, incurable nature of the problem, discuss the benefits and side-effects of therapies, and (when appropriate) allow the client options in treatment selection. Cultivate a relationship with shared patient goals (*e.g.*, is it possible for the cat to live comfortably without an Elizabethan collar?) and encourage communication; when a trusting relationship is forged, the owner will rely on the clinician's expertise and support when setbacks occur.

Anti-inflammatory treatments are the cornerstone of therapy, but consider the phase of therapy when managing patients with cutaneous hypersensitivity. Acute phase treatments rapidly reduce pruritus in patients at commencement of ectoparasiticide therapy and during elimination diet trials, and are also effective for flares of atopic dermatitis. Glucocorticoids and oclacitinib are the most effective acute phase anti-inflammatories. Once the diagnosis of atopic dermatitis is made, transition to chronic maintenance therapy, with the most evidence-based, safe and effective non-steroid long-term options being modified cyclosporine and allergen-specific immunotherapy. If glucocorticoids must be used long-term, aim to use the lowest dose and frequency required to control signs. Once chronic maintenance therapy is instituted, it is wise within the first year to consider rechecking the patient initially once per season to ensure optimal control and for assessment of secondary cutaneous or otic infections. For chronically well-managed cats, consider recheck every 6-12 months, ideally during the patient's more pruritic season.

Glucocorticoid therapy is ideally limited to the acute and diagnostic phases of therapy. The author prefers oral prednisolone therapy to better tailor and taper dosages, and mitigate side effects, when possible. A typical regime might be 1.0-2.0 mg/kg q24H for initial control of pruritus, and tapering to a dose of 0.5 mg/kg q48H as maintenance therapy. However, doses of 2-3 mg/kg/day may be required for control of eosinophilic granuloma complex lesions. Given the risks (*e.g.*, iatrogenic Cushing's, diabetes mellitus, and urinary tract infection), it is prudent to perform a biochemical profile and urinalysis at baseline, 3-4 months after commencement, and every 6 months thereafter or as otherwise indicated given general health status. Recrudescence of cutaneous or ocular herpesvirus may also occur.

Modified cyclosporine is approved in some countries for the treatment of feline atopic dermatitis, and is appropriate for chronic management. The most common side effect is gastrointestinal upset, in approximately 25% of cats, which may be transient or sustained. Given concern for life-threatening systemic toxoplasmosis, particularly in naïve patients, hunting and raw meat consumption is contraindicated. The author recommends a dose of 7.5 mg/kg/day for a trial period of 8 weeks, and once shown to be efficacious, the response may be maintained in some individuals with dosing every 48-72 hours. The drug may be administered in wet food without affecting the pharmacokinetic parameters, which can enhance compliance (10). Although baseline and follow-up bloodwork and urinalysis are prudent, changes in these parameters are rare (11).

Oclacitinib is approved for the treatment of allergic dermatitis in dogs and although off-label, it has demonstrated efficacy (12,13) and safety (14) as both acute and chronic therapy in feline atopic dermatitis. However, reports only extend for up to 28 days, so information regarding long-term safety is entirely anecdotal. Pharmacokinetics in cats support higher and more frequent oral dosing compared to dogs (15), with studies indicating an initial dose range of 0.4-1.0 mg/kg q12H (12,13); once well controlled, once-daily dosing may be attempted. However, the majority of patients are optimally managed on BID therapy long-term. The requirement for frequent tablet administration is a disadvantage for chronic dosing in cats. Given the general lack of safety data, consider baseline blood analysis and urinalysis, and continue monitoring every 3-6 months. In the author's experience, oclacitinib has demonstrated long-term safety and efficacy in cats, but if used, other immunomodulators should be avoided or approached with caution. The author has diagnosed multifocal *D. cati* and pyelonephritis in a cat receiving concurrent oral dexamethasone and oclacitinib for severe atopic dermatitis.

Allergen-specific immunotherapy administered subcutaneously or sublingually is appropriate for prolonged therapy; it is the only treatment that promotes immune tolerance and has no known long-term side effects. Allergens are selected via intradermal and/or serum IgE allergy testing and patient environmental history, but treatment can take up to 12 months for a notable response. To maintain comfort most patients will need ongoing or intermittent anti-inflammatory therapy over this period. Approximately 60% of cats will demonstrate a good medication-sparing or eliminating response (16), with most patients requiring ongoing treatment to maintain tolerance. Client education, including the

desire to reduce the requirement for drug therapy and the need for long-term treatment, is essential to prevent premature discontinuation and associated squandering of financial and time resources.

Antihistamines are inappropriate for acute management given their general lack of efficacy (17) and delayed onset of action. They may be effective as a steroid-sparing medication, or sole therapy in a very narrow population of patients.

Fatty acid therapy is appropriate for chronic management for all patients with atopic dermatitis, and can be sourced in prescription diets for atopic dermatitis, capsules and liquid preparations. By itself it does not significantly reduce pruritus, but may reduce severity of flares, improve skin barrier function with reduced allergen penetration and secondary infection, and has shown to have a drug-sparing effect in canine atopic dermatitis (18). The author recommends eicosapentanoic acid at a minimum dose of 90 mg per day to reduce pruritus in cats with atopic dermatitis.

Eosinophilic granuloma complex lesions are resolved with glucocorticoids and/or modified cyclosporine, but relatively higher initial doses and longer courses of glucocorticoid therapy may be required for remission. Modified cyclosporine alone may resolve lesions although it has a slow onset of approximately 4-6 weeks, but is reliably efficacious for long-term control of eosinophilic granuloma complex lesions. Diagnostic phase patients may continue glucocorticoid treatment to maintain relief during ectoparasiticide and elimination diet trials, but discontinue treatment at their conclusion to interpret trial efficacy. Peer-reviewed studies describing the use of oclacitinib to treat active eosinophilic granuloma complex lesions are lacking, but chronic maintenance oclacitinib or allergen-specific immunotherapy may prevent lesion relapse.

Finally, otitis externa, as previously mentioned, may be in exclusion or may occur in concert with other reaction patterns. Systemic anti-inflammatory therapy and immunotherapy are not reliable means of control. Once secondary infection and inflammation are treated topically, and systemic therapy instituted for cutaneous signs, continue to recheck the ears, and consider maintenance topical steroids once or twice weekly. Ear flushing as maintenance therapy may be helpful, but a discussion of topical otic therapeutics is beyond the scope of this article.

CONCLUSION

Deterioration of quality of life and the significant caregiver burden caused by feline atopic dermatitis must be recognized and addressed whenever possible. Compliant long-term maintenance prevents undue flares, reducing antibiotic and glucocorticoid exposure over time. However, even well-maintained patients can relapse from year to year or season to season, so consider developing a proactive patient-specific treatment and communication plan should a flare occur, and establish a long-term recheck schedule to ensure optimal control.

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THERAPEUTIC OPTIONS FOR THE PRURITIC CAT

The clinician presented with an itchy cat has fewer options than when dealing with a pruritic dog – or is that true? Jay Korbelik offers some ideas backed by clinical studies.

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KEY POINTS

1. Feline atopic dermatitis is currently diagnosed based upon a compatible history and clinical presentation, with exclusion of other pruritic dermatoses.
2. The pruritic cat will present with various signs, including head and/or neck excoriations, symmetrical self-induced alopecia, miliary dermatitis, or eosinophilic granulomas complex lesions.
3. Treatment options available for feline atopic dermatitis are limited when compared to dogs, and may involve off-license drugs.
4. No single treatment is effective in controlling signs of feline atopic dermatitis in all cases, and a multi-modal approach is often necessary.

Introduction

Pruritic disorders in cats are often attributed to hypersensitivity dermatides (HD) including flea bite hypersensitivity (FBH), food-induced hypersensitivity dermatitis (FIHD) and atopic dermatitis (AD) (1). Use of the term feline AD remains debatable because the clinical presentation, histologic features and role of IgE differ significantly to that of human and canine atopy (1,2). The significance of IgE in the pathogenesis of this condition has not been firmly established, and there are currently very few studies that have investigated the role of IgE in feline AD (3). The term non-flea, non-food induced hypersensitivity dermatitis (NFNFIHD) is sometimes used to refer to this condition. Feline AD is suggested to be the second most common HD in cats (4); one study reported a prevalence of 12.5% of all feline dermatoses (2), and also found that Abyssinian, Devon Rex and domestic breed cats were over-represented. Clinical signs typically start manifesting in young cats (under 3 years of age) (5) although one study did find that 22% of cats with feline AD were over 7 years of age (2). This study also found that 93% of cats with feline AD were perceived as being pruritic by their owners, and importantly, trichogram analysis in the remaining 7% confirmed broken hairs consistent with pruritic behavior. The majority of cats (80%) in this study had non-seasonal signs.

Cats with HD will present with one or more of the following patterns: head and/or neck excoriations **(Figure 1)**, symmetrical self-induced alopecia, miliary dermatitis, or eosinophilic granulomas complex lesions **(Figures 2 and 3)** (1,2). Other

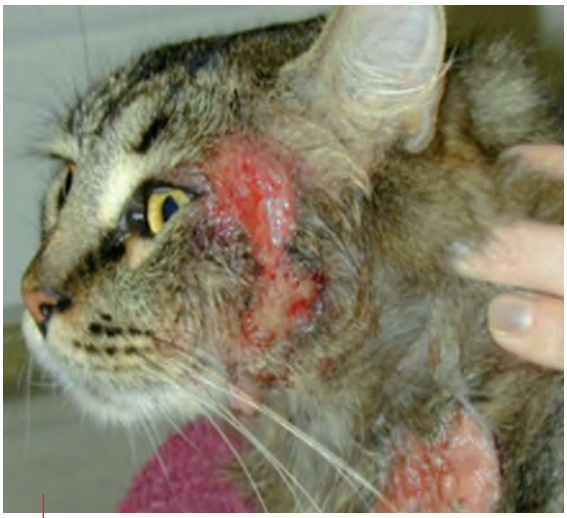

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Figure 1. Head and neck excoriations in a cat with AD.

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Figure 2. A cat with indolent ulcers on the upper lips, a common presentation of lesions associated with the eosinophilic granuloma complex.

presentations, including pododermatitis, facial erythema, seborrheic disorders or ceruminous otitis have also been reported (3,5). It is impossible to distinguish between the different causes of HD based on clinical presentation; although one study found that cats with FIHD were more likely to present with lesions on the head and neck, and cats with FBH were more likely to present with lesions on the dorsal aspect of the body (rump and tail) (1), this finding was not considered statistically significant. **Figure 4** shows the most commonly affected sites of HD with the different causes.

Feline AD is currently diagnosed based upon a compatible history and clinical presentation, along with exclusion of other pruritic dermatoses (5). It is especially important for the clinician to rule out FBH with appropriate ectoparasite treatment and, for cats exhibiting non-seasonal signs, a restricted diet trial (for typically 8 weeks) to rule out FIHD (5). Diagnosing and treating feline AD can be challenging and frustrating for even the most seasoned clinician for several reasons:

- There are currently no widely established clinical diagnostic criteria for feline AD as there are in dogs (6).
- Treatment options available for feline AD are limited.
- It can be notoriously difficult to administer oral medication to cats (5).

This article will discuss some of the pharmaceutical treatment options used to control pruritus caused by AD in feline patients.

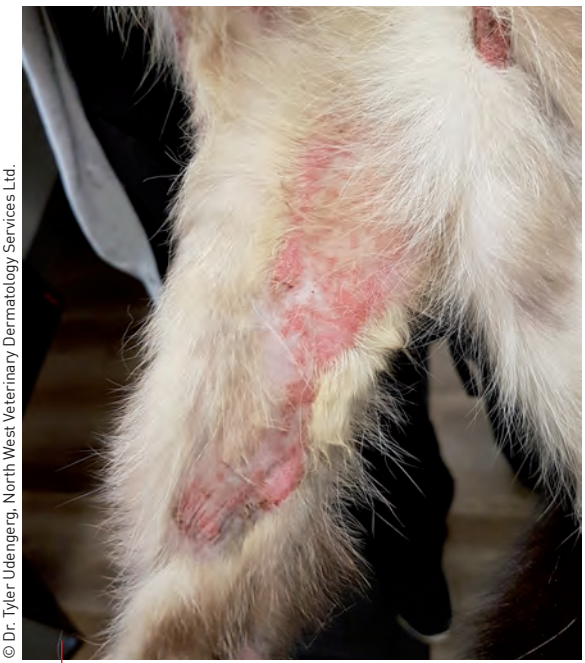

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Figure 3. Eosinophilic plaques in a cat, another common presentation of lesions associated with the eosinophilic granuloma complex.

Corticosteroids

Corticosteroids have long been the mainstay of treatment for feline AD, and are frequently used as cats appear to be generally more resistant to the adverse effects of this class of drugs than dogs (5). Although feline AD has been reported as typically corticosteroid responsive (5), one study found that a good response to systemic corticosteroids was only reported in 55% of cats, although the type, dosage and duration of therapy were not evaluated (2). No studies have examined the most effective way to taper corticosteroids, but an induction dosage is generally employed for the first week and then tapered at 1–2 week intervals, with the aim of attaining the lowest every other day dosage that maintains remission and minimizes side effects (7). In cats, prednisolone is recommended over prednisone due to significantly higher bioavailability (100% vs. 21% respectively) (8). One study showed that methylprednisolone (1.41 mg/kg

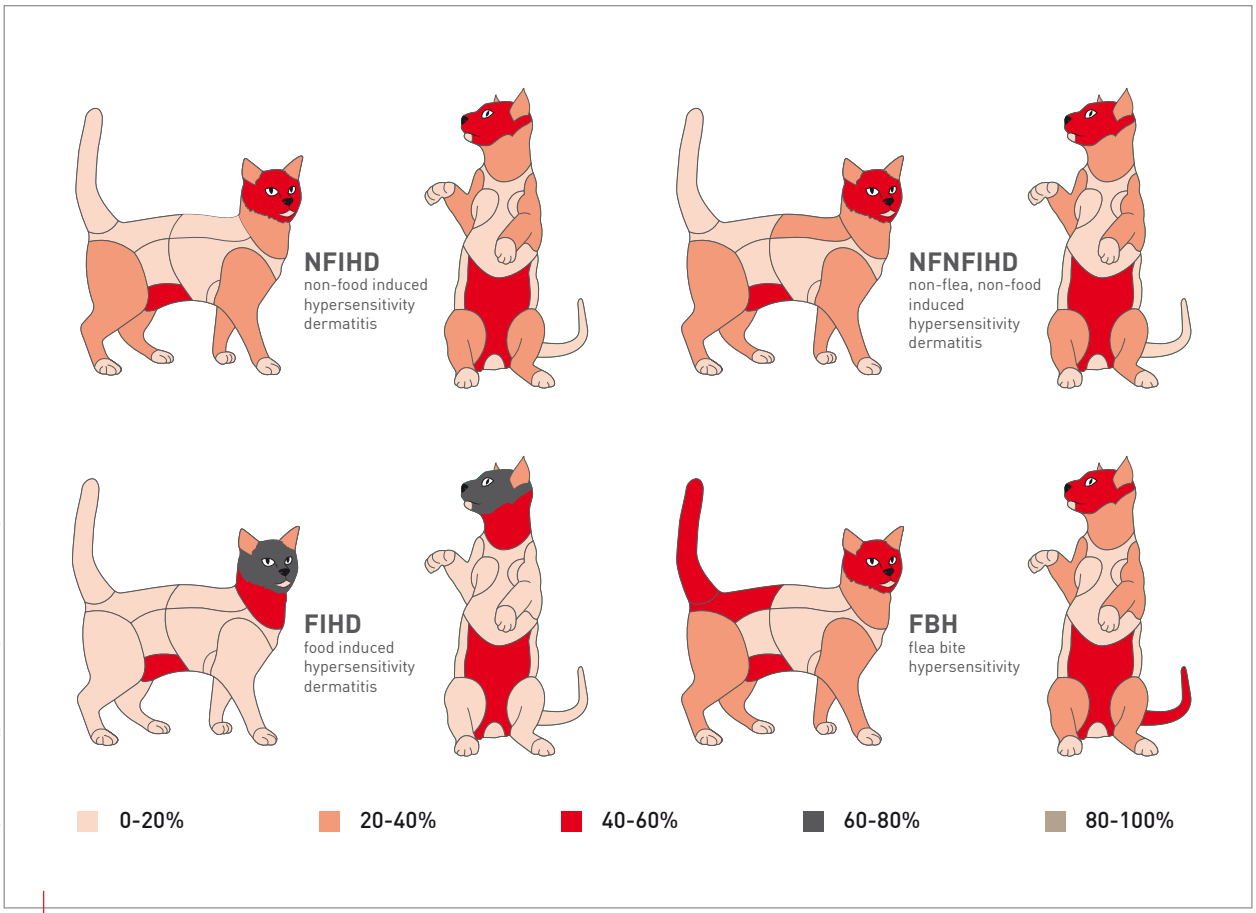

Figure 4. Silhouettes depicting the proportion of distribution of lesions in cats with hypersensitivity dermatides. Reprinted from (1).

q24H) or triamcinolone (0.18 mg/kg q24H) were effective at inducing remission of pruritus in 90.6% of allergic cats within 7-14 days, while prednisolone (1 mg/kg q24H) only achieved remission in 45.5% of cats after 28 days (7). This study also indicated that 0.54 mg/kg q48H of methylprednisolone or 0.08 mg/kg q48H of triamcinolone were effective at maintaining remission in these cats.

Adverse effects of corticosteroid treatment can include marked cutaneous atrophy, congestive heart failure, iatrogenic hyperadrenocorticism and increased risk of diabetes mellitus, among others (9). A preliminary study suggested that dexamethasone exhibited a greater diabetogenic effects in cats than the equivalent dose of prednisolone (10).

For patients that require long-term maintenance therapy, injectable glucocorticoids (*e.g.*, methylprednisolone acetate) are usually not recommended, as oral administration is more precise and is associated with a lower risk for side effects (9). Additionally, a poorly understood but well recognized phenomenon called steroid tachyphylaxis (*i.e.*, resistance) can occur when the drug is administered long-term, and in these cases changing the type of corticosteroid administered can often result in better clinical response (9). Topical corticosteroids, including mometasone furoate and hydrocortisone aceponate, are reported to provide good control of pruritus in some cats, or can be used to reduce the need for systemic corticosteroids (2,9).

Cyclosporine

Cyclosporine is a calcineurin inhibitor with immunosuppressive activity that focuses on cell mediated immune responses (9). Several studies have found good efficacy and safety of cyclosporine to treat feline HD when used at 7 mg/kg q24H PO after 4-6 weeks (2,11-13). One study found that 70% of cats receiving cyclosporine could be reduced to every other day dosing after 4 weeks of treatment, and over the following four weeks 57% of cats could then be reduced to twice weekly dosing (13).
A single study has evaluated the administration of cyclosporine 50 mg/mL subcutaneously; this formulation, given initially at 2.5-5 mg/kg once daily to alternate days, appears to be an efficacious therapy for feline AD and may be an alternative option for cats that cannot be treated orally (14).

Monitoring serum levels of cyclosporine in HD is typically not recommend, as the levels generally do not correlate with clinical response (9). The most commonly observed adverse effects are digestive tract disorders, including vomiting, diarrhea,

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hypersalivation and anorexia (9,11,12), and the resulting weight loss may lead to hepatic lipidosis (9). Most of these adverse effects were mild in nature and did not require withdrawal from the studies (11,12). Giving the drug with a small amount of food or freezing the capsules before administration have been suggested to minimize gastrointestinal side effects (15). Some clinicians recommend giving the liquid preparation of this medication cold to alleviate this adverse effect, although the author is not aware of any studies that have confirmed preparation stability at this temperature.

Rarely, development of severe systemic illness due to *Toxoplasma gondii* has been reported (2,9). Titer testing for *T. gondii* should therefore be consider prior to starting therapy (2), and cats should not be fed a raw food diet or be allowed to hunt while receiving cyclosporine (2). All cats should also be tested for Feline Immunodeficiency Virus (FIV) and Feline Leukemia Virus (FeLV) prior to treatment (9). Many clinicians recommend pre-cyclosporine testing to include complete blood count, biochemistry and urinalysis, and will monitor ongoing treatment every 6-12 months thereafter (9).

Antihistamines

Few studies have evaluated the use of antihistamines to treat pruritus due to feline AD, and dosing recommendations and efficacy vary greatly. Antihistamines generally tend to be well tolerated but have low efficacy (2,16,17). The efficacy of cetirizine has been most widely evaluated, with one study reporting a reduction in pruritus in 41% of cats (16), but another study reported a good response in only 6% of cats and a partial response in 34% of cats (2). However, no statistical difference in reduction of pruritus between cats treated with cetirizine and those treated with a placebo has been reported (17). A retrospective review noted a good response to loratadine treatment in only 5% of cats and a partial response in 42% of cases, although the number of cats in this study was low (2). The efficacy of cyproheptadine hydrochloride was evaluated in one study; pruritus was satisfactorily controlled in only 45% of cats (18), and side effects (including polyphagia, sedation, vocalization, affectionate behavior, and vomiting) were noted in 40% of animals.

Oclacitinib

Oclacitinib is a Janus kinase inhibitor that has primarily been used in the treatment of pruritus in dogs. It can be used off-label in cats, although limited studies have evaluated its efficacy and safety. A pharmacokinetic study of oclacitinib found that larger doses and shorter dosing intervals would be recommended in cats to achieve similar blood concentrations to those in dogs (19). One study reported that oclacitinib was effective at reducing pruritus in 51% of cats and improved clinical lesions of feline AD in 61% of cats when dosed at 1 mg/kg q12H (20). The efficacy of the drug was comparable to methylprednisolone efficacy in this study, with the latter performing slightly better.

Oclacitinib appears to be well tolerated in cats, although one study found that 4 out of 14 cats had a mild increase in kidney function tests after 4 weeks of use (20). A second study evaluating the safety of this drug in cats noted gastrointestinal side effects in a small proportion of cases when given at 2 mg/kg q12H (21). It also noted a small but significant increase in fructosamine levels when cats were treated with oclacitinib, although values remained within the normal reference range. Further investigation is required to evaluate long-term safety of this treatment in cats.

Maropitant

Maropitant is a neurokinin-1 receptor antagonist indicated for the prevention of vomiting and nausea in cats. Its anti-pruritic and anti-inflammatory effect is thought to rely on its ability to inhibit substance P by binding to its receptor (22). In one study, cats were treated with maropitant at 2.22 mg/kg q24H for 4 weeks, resulting in a decrease in both clinical lesions and pruritus scores associated with AD in all animals except one (22). The efficacy and the tolerability of the treatment were judged as excellent or good in 83.3% of cats, with the only side effect being self-limiting sialorrhea in a small number of cases.

Palmitoylethanolamide (PEA)

PEA is a naturally occurring lipid compound with antiallergic and anti-inflammatory effects (23,24). PEA binds to peripheral cannabinoid receptors and down-regulates mast cell degranulation (23). A pilot study on cats with eosinophilic granulomas and plaques showed that 30 days of treatment with co-micronized PEA reduced the severity of clinical lesions and pruritus in more than 60% of cases (23). A second study, in which cats were co- and post-administered ultramicronized PEA (PEA-um) at 15 mg/kg q24H PO, showed that the compound enhanced the anti-pruritic effect of a short course of methylprednisolone treatment, and could delay flares in cats with HD (24). It reported that the cats could be maintained relapse- and corticosteroid-free for a mean period of six weeks with no serious side effects, although mild gastrointestinal upset was noted.

CONCLUSION

No single treatment is effective in controlling signs of feline atopic dermatitis (AD) in all cases and a multi-modal approach is often necessary. As this article focuses on pharmaceutical treatment options of feline AD, allergen-specific immunotherapy is not discussed, but this option certainly plays a role in management of this condition. As feline AD is an incurable condition that requires life-long management, the clinician must always weigh the potential side effects of treatment with the benefit. Further study is needed to develop a diagnostic criteria for feline AD, along with investigation into its pathogenesis and potential treatment options.

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