The nomenclature for feline cutaneous allergic skin disease has been recently updated. In the past, the term feline hypersensitivity dermatitis was widely used for cutaneous allergic reactions resulting from flares triggered by flea, food, and environmental allergens. The term feline hypersensitivity dermatitis has been replaced with feline atopic syndrome (FAS), which broadly includes feline allergic skin disease, food allergy, and/or asthma. Within the new FAS nomenclature, feline atopic skin syndrome (FASS) refers explicitly to allergic skin disease induced by environmental allergens (e.g., dust mites, pollens, molds). This short review focuses on FASS.

FASS is a common pruritic and inflammatory skin disease of cats. In a large multicenter study on pruritic cats, FASS represented 20% of the study cats, making it one of the most prevalent skin diseases among cats. Manifestations of pruritus in cats are scratching, rubbing, chewing, licking, and/or excessive grooming. Cats with diagnosed FASS typically exhibit 1 or more of the following clinical lesion patterns: miliary dermatitis, self-induced symmetrical alopecia, facial head and neck pruritus with excoriations and erosions, and eosinophilic granuloma complex.

- **Miliary dermatitis** is characterized by multiple erythematous papules that are covered by small crusts typically centered around the neck and, in some patients, may be more visible in the sparsely haired preauricular space (FIGURE 1A).

- **Self-induced symmetric alopecia** results from overgrooming and is commonly seen on the abdomen, limbs, and flanks (FIGURE 1B).

- **Facial head and neck pruritus** results from excessive scratching around the head and neck, leading to excoriations and erosions. Alopecia and miliary dermatitis can also be associated with this clinical presentation (FIGURE 1C).

- **Eosinophilic granuloma complex** encompasses 3 clinical forms: indolent ulcer, eosinophilic plaque, and granuloma. An indolent ulcer, frequently referred to as a rodent ulcer, appears as an ulcerative lesion of...
the upper lip; the lesion may be unilateral or bilateral and may become quite large when chronic. An eosinophilic plaque is an elevated, erythematous, and often eroded-to-ulcerative lesion most commonly found on the ventral abdomen and medial thighs (FIGURE 1D). Eosinophilic granuloma can appear as a linear, firm lesion most often on the caudal aspect of the hind limbs, a diffuse swelling of the chin, and/or a proliferative lesion in the mouth.

In many studies, most cats with FASS were around 3 years of age or younger and females seemed to be overrepresented. Although seasonality often plays a role in FASS, nonseasonal signs develop over time in a large percentage of cats.

**DIAGNOSTICS AND DIFFERENTIAL DIAGNOSES**

There is no specific single finding or test for FASS;
rather, the diagnosis is based on history, clinical examination findings, exclusion of other pruritic dermatoses, and fulfillment of published diagnostic criteria for FASS.\textsuperscript{3,4}

Excluding Other Causes of Pruritis
Because ectoparasites such as \textit{Notoedres}, \textit{Demodex} (i.e., \textit{Demodex gatoi}), and \textit{Otodectes} mites can result in pruritus, diagnostics such as superficial skin scrapings, hair plucks, and examination of otic debris should be performed where appropriate.\textsuperscript{4} An important differential for FASS is flea allergy dermatitis, which necessitates effective adulticidal flea control for the affected cat, any in-contact animals, and the patient’s environment for a minimum of 9 weeks.\textsuperscript{4}

Complication features in cats with FASS are bacterial pyoderma and \textit{Malassezia} overgrowth, both of which can contribute to pruritus. Skin cytology is simple to perform, and identification and treatment of secondary infections aid in the management of these patients.\textsuperscript{4}

Diagnostic Criteria
Criteria have been established to help with diagnosing food- and/or environment-induced FAS (previously described as non–flea-induced hypersensitivity dermatitis) after flea hypersensitivity has been excluded (BOX 1).\textsuperscript{3} When 6 of these 10 criteria are met, the sensitivity is 90\% and specificity is 83\%.\textsuperscript{3} Although these criteria help differentiate FASS from other causes of pruritus, there is no current means to discriminate FASS from a food allergy.\textsuperscript{3,4} A food allergy can mimic any of the 4 clinical lesion patterns observed in FAS, and as such, an elimination diet trial using either a novel limited ingredient or a hydrolyzed diet should be performed for a minimum of 8 weeks.\textsuperscript{4,6} Suggestive of a food allergy are extracutaneous signs involving the gastrointestinal system (vomiting, diarrhea, flatulence) and/or conjunctivitis and/or an older patient in which 1 or more of the clinical lesion patterns develops.\textsuperscript{4}

During the first 5 to 6 weeks of the elimination diet trial, treatment of any secondary skin/ear infections along with resolution of pruritus is necessary before medications can be discontinued and the patient reassessed solely on the diet. If clinical relapse is not noticed within 2 weeks, rechallenge with the previous diet should be performed. Return of clinical signs within 7 days of rechallenge confirms a food allergy diagnosis for 90\% of cats and for almost all cats within 14 days.\textsuperscript{7} Although FASS and a food allergy can be diagnosed for the same patient, a recent review reported that incidence of both conditions is very low (2.4\%).\textsuperscript{4}

Intradermal and IgE Testing
No type of allergy testing, whether intradermal and/or serologic allergen-specific IgE testing, should be used to diagnose FASS. Multiple studies have shown no significant differences in measured serum levels of IgE between allergic cats and healthy controls.\textsuperscript{8,9} In addition, increasing serum levels of IgE have been shown to correspond with age, residing outdoors, and absence of deworming.\textsuperscript{8} Interpreting results of intradermal skin testing of cats can be challenging due to weak reactions; intravenous fluorescein dye has been recommended to help visualize responses with use of a Wood’s lamp.\textsuperscript{4} Because avoidance of environmental allergens such as pollens is often impractical, allergy testing and allergen-specific immunotherapy can play a role in the long-term management of cats with FASS. However, allergy testing should only be used to identify allergens in patients undergoing allergen-specific immunotherapy (AIT) and desensitization rather than to diagnose an “allergic cat.”

\textbf{BOX 1 Diagnostic Criteria for Feline Atopic Syndrome (Food- and/or Environment-Induced)*}

\begin{itemize}
  \item \textbf{Presence of}
    \begin{itemize}
      \item Pruritus at onset
      \item At least 2 of the following classic clinical reaction patterns:
        \begin{itemize}
          \item miliary dermatitis
          \item symmetric alopecia
          \item head and neck erosions/ulcerations
          \item eosinophilic dermatitis
        \end{itemize}
      \item At least 2 sites affected
      \item Miliary dermatitis as a dominant pattern
      \item Eosinophilic dermatitis, symmetric alopecia, or erosions/ulcerations on the head, face, lips, ears, or neck
      \item Nonsymmetric alopecia on the rump, tail, or hindlimbs
      \item Symmetric alopecia on the abdomen
    \end{itemize}
  \item \textbf{Absence of}
    \begin{itemize}
      \item Erosions/ulcerations on the forelimbs
      \item Lesions on the sternum or axilla
      \item Nodules or tumors
    \end{itemize}
\end{itemize}

*The term feline non-flea-induced hypersensitivity dermatitis used in reference 3 has now been replaced with feline atopic syndrome.
TREATMENT OF FASS

FASS frequently requires medical therapy, which can present compliance challenges for the patient and the client. Although a recent extensive review proposes several treatments for managing FASS,10 this article reviews use of glucocorticoids, cyclosporine, oclacitinib, and AIT.

Glucocorticoids

The drugs most commonly used to manage FASS are systemic glucocorticoids due to their broad-range anti-inflammatory effects. Systemic glucocorticoids rapidly and effectively ameliorate pruritus and skin lesions in cats with FASS.10,11 A recent study demonstrated a marked (>50%) reduction in pruritus and lesional skin scores (SCORing Feline Allergic Dermatitis [SCORFAD], pubmed.ncbi.nlm.nih.gov/22823903) in FAS cats given dexamethasone sodium phosphate (4 mg/mL) at 0.2 mg/kg PO for 20 to 31 days without significant adverse effects.12

Other glucocorticoids that have shown efficacy in treating allergic cats include triamcinolone and methylprednisolone; mean oral daily induction doses were 0.18 mg/kg and 1.41 mg/kg, respectively.13 Subcutaneous injections of methylprednisolone acetate may seem to be an attractive treatment option for feline patients with refractory FASS and for which oral administration of tablet-type medications is challenging. However, the lack of prospective controlled studies evaluating the dosages, frequency of administration, and efficacy in cats with FASS,13 as well as possible side effects including iatrogenic hyperadrenocorticism,14,15 suggests a need for careful evaluation of the pros and cons of this treatment.

Cyclosporine

Cyclosporine is a calcineurin inhibitor that inhibits T-cell activation.15 The recommended dosage for cats with FASS, based on 2 randomized, double-blinded, placebo-controlled studies, is 7 mg/kg PO q24h.16,17 In one study, after 42 days of treatment with cyclosporine at the 7 mg/kg PO q24h dosage, the average decrease in total lesion score was 65.1% for 144 cats with FASS compared with 9.2% for the 73 placebo group cats.17 Although the veterinary formulation of cyclosporine (Atopica; Elanco, elanco.us) has been routinely administered to FASS patients, human formulations have also been successfully used for management of FASS.18

When prescribing human cyclosporine, it is imperative to use only the microemulsified (i.e., modified) product because oral bioavailability of this product in both human and veterinary patients is greater than that of the vegetable oil formulation, which is not modified.19 A new liquid formulation of cyclosporine for dogs (Cyclavance; Virbac, vet-us.virbac.com) could potentially be used in an off-label manner for cats as well. After clinical remission has been achieved with cyclosporine, the success rate for tapering the drug to every other day is up to and greater than 70% for FAS cats and greater than 50% for FAS cats when further lowered to twice weekly.20,21 According to multiple studies, the most common side effect of cyclosporine in cats is gastrointestinal disturbance (vomiting, diarrhea),16-18 which lessens with continued use and frequency.20,21

Oclacitinib

Oclacitinib (Apoquel; Zoetis, zoetisus.com), a Janus kinase inhibitor registered for use in dogs with allergic dermatitis,22 has recently garnered a lot of attention in the treatment of FASS. Although the drug is not labeled for use in cats, it has been evaluated in several studies; however, comparing efficacy among the studies is challenging as the dosages used were not the same.23-25 In a recent study, oclacitinib was found to be as efficacious as methylprednisolone for reducing pruritus and skin lesion scores after 28 days.26 Another study found that oclacitinib at 1 mg/kg PO q12h seems to be safe in cats for at least 28 days without significant laboratory abnormalities requiring medical intervention.26 Because the half-life of oclacitinib is shorter in cats (2.3 hours) than in dogs (4.1 hours),27 the current recommended oclacitinib dosage for cats is 1 mg/kg q24h to q12h with informed owner consent along with diligent monitoring.10 Long-term studies looking at the safety of oclacitinib in cats with FASS are needed.

Allergen-Specific Immunotherapy

Allergen-specific immunotherapy is the only treatment for FASS that has the potential to induce tolerance and enable reduction or complete elimination of other long-term treatments.28 Mechanisms of tolerance demonstrated in humans include induction of regulatory T (Treg) cells leading to increased levels of interleukin-10 and transforming growth factor-β, resulting in decreased T helper 2 (Th2) cytokines.29 Lower levels of Th2 cytokines lead to decreased
Allergen-specific immunotherapy is the only treatment for FASS that has the potential to induce tolerance and enable reduction or complete elimination of other long-term treatments.  

degranulation and tissue infiltration of mast cells, basophils, and eosinophils. AIT also induces production of IgG4, which leads to reduced production of allergen-specific IgE. As to whether these mechanisms of inducing tolerance are applicable to cats requires further investigation. AIT has traditionally been administered to cats subcutaneously or sublingually; in a recent study that evaluated sublingual administration to 22 cats with feline atopic dermatitis for 1 year, all 16 cats that completed the study showed marked improvement in skin lesions after only 3 months. Furthermore, of 7 cats that required oral methylprednisolone at the beginning of the study, discontinuation of this medication was possible for 3 cats and reduction by more than 50% was possible for the other 4 cats by the end of the study.

Other Treatments

Other products used to treat pruritus and skin lesions in cats include antihistamines, maropitant citrate, essential fatty acids, and palmitoylethanolamide.

**TAKE-HOME POINTS**

- Feline allergic disease has undergone a recent change in terminology. Feline atopic skin syndrome (FASS) refers explicitly to allergic skin disease induced by environmental allergens.
- The major components of FASS are pruritus and inflammation.
- FASS treatment requires a partnership with the client and tailoring of treatments to the individual patient.
- Further study is needed to elucidate the pathogenesis of FASS and the development of more targeted and beneficial therapies. **TVP**

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References

23. Noi C, Matriccioni S, Schieveano C. A double-blinded, randomized, methylprednisolone-controlled study on the efficacy of oclacitinib


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Dr. Vargo is a dermatology resident at the University of Georgia. After graduating from the Western College of Veterinary Medicine (WCVM), Saskatoon, Saskatchewan, Canada, in 1999, she was in general practice for 4 years before completing a rotating internship in Greensboro, North Carolina, followed by a residency and a Master of Veterinary Science degree in small animal internal medicine at WCVM. Dr. Vargo obtained ACVIM Diplomate status in 2008 and worked in private specialty practices and at WCVM before pursuing a dermatology internship in 2019 and a Master of Science degree in comparative biomedical science. Dr. Vargo’s main interests are feline and canine atopic dermatitis, canine necrolytic migratory erythema, and autoimmune skin diseases.

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Brief Summary: Before using NexGard® (afoxolaner) Chews, please consult the product insert: a summary of which follows.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description: NexGard is a soft chewable for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/ lb (2.5 mg/kg).

indications: NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis), and the treatment and control of lice infestations (Psoroptes cuniculi, Dermanyssus gallinae, and Sarcoptes scabiei) in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. Nexgard is indicated for the prevention of Borelia burgdorferi infections as a direct result of killing Ixodes scapularis vector ticks.

Dosage and Administration: NexGard is given orally once a month, at the minimum dosage of 1.14 mg/lb (2.5 mg/kg). See full product insert for dosing table and details.

Warnings: Not for use in humans. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a physician immediately. Keep NexGard in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions: Afoxolaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated.

Adverse Reactions: In a well-controlled US field study, which included a total of 333 households and 615 treated dogs (415 administered afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard.

Over the 90 day-study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported at an incidence of > 1% within any of the three months of observations are presented in the following table.

Table 1: Dogs with Adverse Reactions

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Afoxolaner</th>
<th>Oral active control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N°</td>
<td>% (n=415)</td>
<td>N°</td>
</tr>
<tr>
<td>Vomiting (with and without blood)</td>
<td>17</td>
<td>4.1</td>
</tr>
<tr>
<td>Dry/Flaky Skin</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Diarrhea (with and without blood)</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Lethargy</td>
<td>7</td>
<td>1.7</td>
</tr>
<tr>
<td>Anorexia</td>
<td>5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

1 Number of dogs in the afoxolaner treatment group with the identified abnormality.

2 Number of dogs in the control group with the identified abnormality.

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced a third seizure one week after receiving the third dose. The dog remained enrolled and completed the study. Another dog with a history of seizures had a seizure 19 days after the third dose of NexGard. The dog remained enrolled and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

Post-Approval Experience (July 2018): The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship product exposure using these data. The following adverse events were reported for dogs listed in decreasing order of reporting frequency for NexGard: Vomiting, pruritus, lethargy, diarrhea (with and without blood), anorexia, seizures, hyperactivity/resediveness, panting, erythema, ataxia, dermatitis (including rash, papules), allergic reactions (including hives, swelling), and tremors.

Effectiveness: See full product insert for details regarding Effectiveness.

Animal Safety: In a margin of safety study, NexGard was administered orally to 8 to 9-week-old beagle puppies at 1, 3, and 5 times the maximum exposure dose for a total of six treatments. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistry, or coagulation tests), gross pathology, histopathology, or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment. In a well-controlled field study, no adverse reactions were observed from the concomitant use of NexGard with other medications.

Contact Information: For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae. The information provided here is not comprehensive. The full FDA-approved product insert is available at www.nexgardfordogs.com. Consult your veterinarian for further information.

Product approved by FDA under NADA # 141-406

Marketed by: Frontline Vet Labs™, a Division of Boehringer Ingelheim Animal Health USA Inc. Duluth, GA 30096

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