Flea allergy in dogs: Clinical signs and diagnosis

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SUMMARY

Flea allergy is a very common pruritic dermatological condition in the dog. This dermatitis occurs in young adult dogs of any sex. Certain breeds may be predisposed. Clinical signs are usually more severe during the warm season. They are characterised by a pruritic erythematous papular eruption affecting the caudal aspect of the dog. Dorsolumbar pruritus and lesions are characteristic diagnostic criteria. With time, lichenification, hyperpigmentation, scaling and crusts appear gradually. Recurrent pyotraumatic dermatitis in the dorsolumbar area, and fibropruritic nodules and crusted papules in the umbilical area may be particularly suggestive of flea allergy dermatitis. Secondary infections are common. Demonstration of fleas or their feces can be difficult because flea allergic dogs remove them from their hair coat during excessive grooming. A flea comb can greatly improve this examination but a negative search should not rule out this hypothesis. Whatever the test used (live flea challenge, intradermal skin testing with flea extracts, *in vitro* serological or cellular test) allergy testing is controversial in the diagnosis of flea allergy dermatitis because of its poor reliability. Although not perfect, a clinical approach combining thorough history and physical examination, elimination of other differentials and response to strict anti-flea treatment is adopted by most authors.

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Introduction

Flea allergy dermatitis (FAD) is one of the most common small animal dermatological conditions and probably the most common pruritic dermatosis in these species. This is particularly true in areas of the world where fleas are endemic, i.e. where fleas find the optimal environment in which to proliferate: low-altitude geographical location, a temperature of approximately 23°C and a relative humidity of 78% [1]. Frequently, clinical signs associated with flea infestation are mild with low to moderate pruritus, the intensity of which is directly correlated to flea burden. Simple infestation is not associated with hypersensitivity reactions. On the other hand, in flea allergy dermatitis, clinical signs and pruritus are not related to the parasitic load and may be extremely severe. Suggestive historical and clinical data sustain the diagnosis of flea allergy dermatitis. In the 1980's, intradermal skin testing with flea extracts documenting sensitisation introduced many veterinary practitioners and dermatologists to dermato-allergology [2] and for decades, a positive reaction with this test was required to make a definitive diagnosis of flea allergy dermatitis [3].

Historical findings

Suggestive historical data include the presence and/or recurrence of a pruritic dorsolumbar dermatitis in young adult dogs. FAD can occur in animals of any age although clinical signs rarely develop in animals under 6 months of age [4]. The most common age of onset is 3 to 5 years [3]. There is no sex or breed predilection although one study showed a breed predisposition in Chow-Chows, Labrit, Pyrenean Shepherd dogs, Setters, Fox-terriers, Pekinese and Spaniels [5].

Pruritus may or may not be seasonal, depending on the geographical location and climate. Even when pruritus is year-round, clinical signs are usually more severe during the warm season. Owners may report onset or increase in pruritus following the introduction of a new pet, or visit to a boarding or grooming facility [6].

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Initially, corticosteroids produce a marked but temporary remission [7].
The presence of fleas reported by the owner reflects only infestation. In-contact animals, particularly cats, can also be infested and are sometimes the source of infestation.

Clinical signs

Canine flea allergy dermatitis is characterised in its early stages by a pruritic, erythematous and papular dermatitis affecting the caudal aspect of the dog. Lesions are confined to the dorsolumbar area, inner and posterior thighs, ventral abdomen and flanks (Fig. 1) [3]. FAD is the only known canine pruritic dermatitis that consistently affects this region [8, 9] even though one study showed dorsolumbar involvement in only 76% of flea-allergic dogs. Furthermore, the dorsolumbar region was involved in 39% of atopic dogs. In this study, 34% of dogs with FAD exhibited facial pruritus and lesions but the feet were involved in only 1.2% [10]. Whether these signs were related to an adverse food reaction and/or atopic dermatitis or to FAD could have been evaluated for example, by using appropriate flea control. It must be emphasised that atopic status may predispose to flea allergy dermatitis [1, 4]. Another study evaluated the diagnostic value of some clinical clues in the diagnosis of flea allergy dermatitis: it was found that dorsolumbar involvement (lesions and pruritus) was a discriminating diagnostic criterion. Its sole presence in a pruritic dermatitis has a sensitivity of 92% and a specificity of 84% when compared to response to strict flea control [9]. Sometimes, particularly in severely hypersensitive dogs, lesions become generalised and may mimic scabies [3].

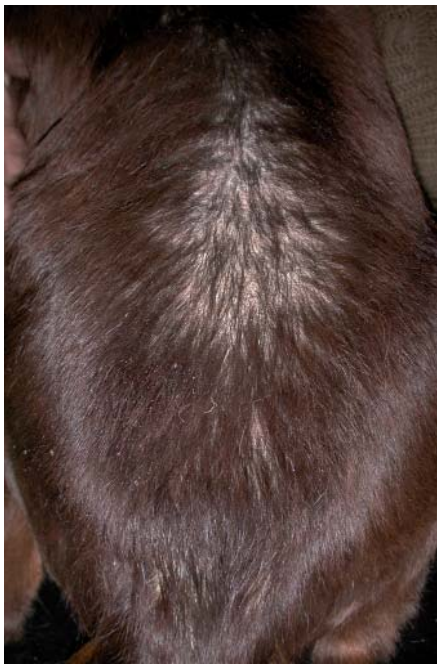


Fig. 1 Alopecia and scaling in the dorsolombar area in a flea allergic dog.

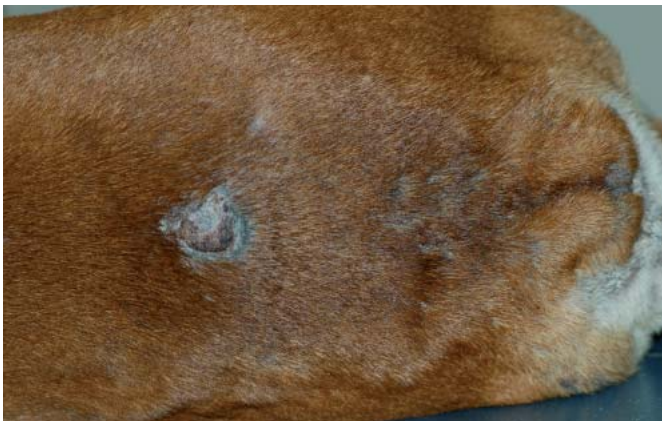
Fig. 3 Brownish stain of the hairs in the dorsolombar area of a flea allergic West Highland White terrier.

Lesions consist of erythema and papules that may become crusted. Crusted papules in the umbilical area may be particularly suggestive of flea bite allergy, especially in male dogs [3, 8]. Pruritus is associated with self-induced alopecia, excoriations, pyotraumatic dermatitis, and a dull and coarse hair coat [6]. Flea allergy dermatitis could be the underlying cause of a majority of recurrent pyotraumatic dermatitis cases arising in the dorsolumbar region in dogs with a dense hair coat (Fig. 2) [3, 9]. In dogs with a light coat colour, hair is stained brown from licking and saliva (Fig. 3) [9].

With time, lichenification and hyperpigmentation, crusts and scaling appear gradually. Fibropruritic nodules may also occur in some chronic cases, usually in the dorsolumbar area. They represent a highly characteristic clinical marker of flea allergy dermatitis in susceptible dogs [8, 9]. Possibly more frequent in old (over 8 years old) German Shepherd dogs with chronic flea allergy dermatitis, they consist of multiple, firm, alopecic and sometimes pedunculated nodules (diameter from 0,5 to 2 cm) (Fig. 4) [9].

Fig. 2 Pyotraumatic dermatitis in a flea allergic dog: alopecia, erosions, erythema and oozing in the flank region

Fig. 4 Pruritic and fibrotic nodule in a flea allergic boxer.



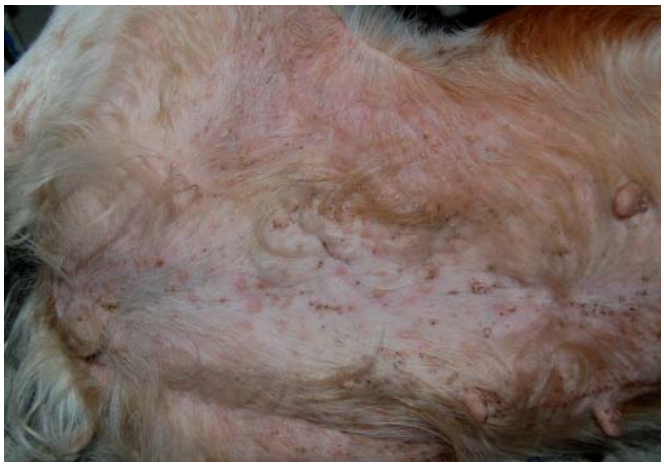


Fig. 5 Bacterial folliculitis in a flea allergic dog: erythema, papules, pustules, crusts and eipdermal collarettes.

Fig. 6 Flea feces dissolving to form brown stain on a wet piece of blotting paper.

Secondary infections such as superficial bacterial folliculitis or *Malassezia* dermatitis are common [3]. They increase inflammation and pruritus. *Malassezia* dermatitis seems to be less frequent in dogs with flea allergy dermatitis than in dogs with atopic dermatitis but secondary superficial bacterial folliculitis is commonly noted (Fig. 5) [9].If corticosteroids are used for long-term pruritus management, superficial bacterial infection can lead to deep pyoderma with furunculosis in the dorsolumbar area [3, 9].

In severely infested dogs, clinical anaemia may be present [3].
Due to the fastidious grooming induced by pruritus, some dogs can ingest adult fleas carrying the tapeworm *Dipylidium caninum* and may have segments of it in their faeces or around the anus [3].

Demonstration of fleas

Close examination of the skin and hair coat may reveal the presence of adult fleas or flea faeces. This can be difficult, sometimes impossible because flea-allergic dogs scratch and lick themselves more than other dogs, removing fleas from their skin and hair coat. The reliability of this examination can be considerably improved by using a flea comb. Combing for a few minutes, especially in lesional areas, after applying an insecticidal spray can help reveal adult fleas. Even if adult fleas are not found, it is sometimes possible to demonstrate flea faeces. These small, reddish-brown comma-shaped fragments, [11] made from haemoglobin crystals, will readily dissolve to form reddish-brown stains if placed on a wet piece of blotting paper (Fig. 6). They can also be examined under the microscope to reveal their characteristic colour and shape.

Human infestation with young adults, recently emerged from their cocoons, may be an indirect sign of a severely infested environment.

In many instances, neither fleas nor flea faeces will be demonstrated but this should not be used to rule out a diagnosis of flea allergy dermatitis if clinical suspicion is high. In a French study, fleas were observed in only 65% of flea-allergic dogs. In 15% of these cases, neither fleas nor flea faeces were found [12].

Differential diagnosis

The differential diagnosis includes all pruritic dermatoses. The most common differentials are bacterial folliculitis, *Malassezia* dermatitis, scabies, trombiculosis, cheyletiellosis, pediculosis, demodicosis, adverse food reaction and atopic dermatitis. Sometimes diagnosis is made difficult by the association of flea allergy dermatitis with one of these other dermatoses, especially bacterial folliculitis and/or *Malassezia* dermatitis [3].
Histopathological examination of skin biopsies reveals superficial perivascular inflammation with variable eosinophilia. This pattern can be seen in other hypersensitivity reactions [13] and is non-specific.

Blood eosinophilia and anaemia are sometimes reported [3].

Allergy testing

Provocative tests are considered to be the gold standard in allergy testing, particularly for food or contact hypersensitivity. They have also been used in flea allergy dermatitis diagnosis (live flea challenge tests), especially to compare the diagnostic value of different assays [14].

A few, newly-emerged, unfed fleas are placed in a universal container the open end of which is covered by a gauze lid, through which the fleas can feed. This container is held for 15 to 20 minutes against the clipped skin of the dog to be tested, usually the skin of the lateral thorax. The container is then removed. The fleas are killed and then crushed to ensure that they contain ingested blood, confirming feeding and exposure of the dog to flea saliva allergens. The challenge site is inspected at 15/20 minutes for evidence of immediate reactivity, then at 24h and/or 48h. Possible lesions include erythema, papules, skin thickening, oedema, wheals, crusts or a combination thereof [14, 15].

Fig. 7 Intradermal skin testing with flea extracts (lecture at 20 min): from top left to bottom right, negative control, positive control, biophady extract, Greer extract, pure flea saliva, Cte f1(2 dilutions).

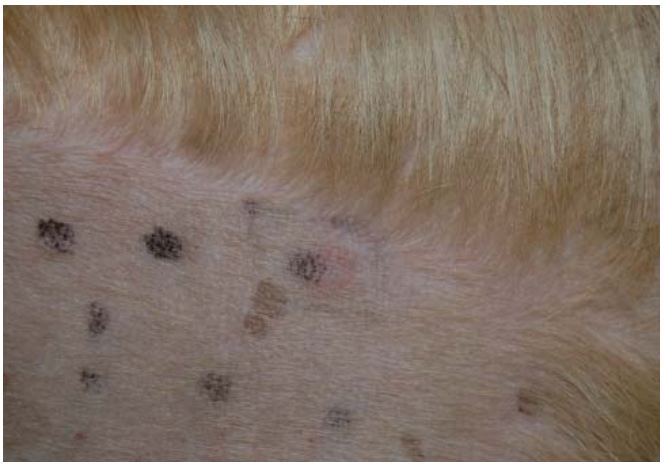


Fig. 8 Intradermal skin testing with flea extract (lecture at 48h): erythematous papule.

These provocative exposure tests are practical on a research basis, but not for most veterinary practitioners and dermatologists. Moreover, their reliability is not excellent: in a study where they took into account only immediate reactions after provocative exposure, Stolper *et al.* showed that sensitivity of this reference test was only around 50% although specificity was excellent (94%). [15]

Allergenic extracts of Ctenocephalides felis felis

Whole-body flea extracts

Allergenic extracts used for immunotherapy and *in vivo* and *in vitro* diagnosis are whole-body flea extracts. They are produced after crushing of the flea bodies, protein extractions and purification. They are not biologically standardised; their composition and allergenicity may vary, altering diagnostic reproducibility and therapeutic efficacy. Furthermore, cross-reactivity to other insect antigens has been demonstrated [16]. A few studies have tried to identify the allergens included in these extracts: several proteins with molecular weights between 14 and 150kδ have been isolated [14, 16]. Purified fractions of these could be less active [15].

Flea Salivary extracts

An artificial flea feeding system on membranes has allowed the *in vitro* collection and purification of flea saliva. Several antigenic fractions have been isolated but results from different studies are controversial. Lee *et al.* isolated 2 proteins with molecular masses of 8-12 kδ and 40 kδ [18]. Franck *et al.* isolated 15 fractions, some of which could elicit a positive immediate intradermal test reaction in sensitised dogs [19]. One of these proteins with a molecular mass of 18 kδ was then cloned and expressed to produce a recombinant allergen; rCte f1 could be a major allergen of flea saliva as IgE directed against this protein has been detected in 95% of experimentally-induced flea-allergic dogs. In naturally occurring flea-allergic dogs, IgE directed against Cte f 1 were detected in only 80% of dogs [20].

Intradermal skin testing

Intradermal skin testing with flea extracts is used to demonstrate in vivo immediate (at 20 minutes) and/or delayed (at 48h) hypersensitivity reactions. Non-standardised whole-body extracts of *Ctenocephalides felis felis* at a concentration of 1:1000 (W/v) are currently the only flea allergens commercially available for intradermal skin testing.

The intradermal skin testing protocol for flea extracts is the same as that for aeroallergens. It requires experience and practice to avoid the most frequent causes of false positive and false negative reactions. For example, all drugs that could interfere with testing must be withdrawn for a suitable length of time prior to the intradermal test (3 weeks for oral and topical glucocorticoids, 8 weeks for injectable glucocorticoids, 10 days for antihistamines, and 10 days for products and diets containing w3/w6 fatty acids)[3]. It seems that even a short administration of glucocorticoids could strongly decrease delayed reactions at 48h [1]. Secondary infections should be cleared and stressed dogs can be anaesthetised.

Dogs are placed in lateral recumbency and clipped carefully over the thorax. After the area has been cleaned with ether, injection sites are marked with a felt-tip pen. Each solution (0.05 mL) is injected strictly intradermally in a standard order, equidistant to the others. Two controls are used: a positive control (histamine phosphate 0.01%) and a negative control (phenolated physiological diluent).

Reactions are first read after 15/20 minutes in the dark with the aid of an oblique light source. A raised erythematous wheal is considered a positive reaction. If erythema is absent, the result is considered negative, even if a small wheal is visible. The greatest diameter of each reaction is measured precisely using a ruler provided by the allergen suppliers. To be considered positive, the diameter of the wheal at the suspected allergen injection site has to be greater than or equal to the mean of the wheal diameters at the histamine and diluent control sites (Fig. 7).

When the reaction read at 15/20 minutes is negative, a second measurement is made at 48h. This interval is considered optimal because the immediate reaction can sometimes persist for up to 24h. Moreover, in a delayed reaction, maximal development of a cutaneous lesion provoked by intradermal injection of an antigen in a sensitive dog occurs between 12 and 72 h [11]. The delayed reaction to flea extract appears as a skin thickening (detected by palpation of a skin fold) or as a papule, both of which can be encrusted (Fig. 8) [4].

The majority of dogs show an immediate reaction followed by a delayed reaction. Halliwell and Gorman demonstrated that 60% of dogs show an immediate and a delayed reaction, 25% only an immediate reaction and 14% only a delayed reaction [4]. For others, the percentage of delayed reactions can be as high as 33% [2].

Whatever the immediate and/or delayed reaction, a positive reaction only means that the dog is sensitised to flea extracts and does not prove that the dermatological problem the clinician is dealing with is flea allergy dermatitis. Results of intradermal skin testing have always to be interpreted in the light of history and clinical signs [3].

Reports of reliability of intradermal skin testing using whole-body flea allergens for the diagnosis of canine flea allergy dermatitis vary greatly. Although some authors report that they give reliable results [2, 3], most of them report poor reliability with sensitivity varying between 70 and 80% and specificity around 60% [21]. This controversy is in part linked to the fact that results vary considerably between studies, one reason for this being whether or not delayed reactions were taken into account.

It must be emphasised that positive reactions may be observed in clinically normal dogs. In Florida, a flea-rich environment, immediate positive reactions have been detected in 24% of clinically normal dogs [22]. Furthermore, this was not predictive of the future development of flea allergy dermatitis as two years later, only 2.5% of these dogs had developed clinical signs of flea allergy dermatitis. However, in Norway, a flea-scarce environment, only 2% of clinically diagnosed "atopic dermatitis" dogs and no clinically normal dogs or dogs with dermatoses other than atopic dermatitis had positive reactions to flea [23]. Positive reactions against flea allergens in atopic and clinically normal dogs in a flea-rich environment might represent truly false positive reactions, subclinical hypersensitivity [22] or cross-reactivity to other insect antigens [16]. This poor specificity has led some authors to abandon intradermal skin testing with flea extracts as a diagnostic tool for flea allergy dermatitis.

Furthermore it seems that not all commercially available flea extracts have the same diagnostic value. One study showed that sensitivity varied between 27 and 67% and specificity varied between 83 and 90% when whole-body flea extracts were used as reagents for intradermal skin testing. When pure flea saliva was used, sensitivity raised to 93% and specificity 90%. The results of intradermal tests comprising immediate and delayed reactions were compared to clinical diagnosis of flea allergy dermatitis based on history, clinical signs and response to strict flea control [7]. This result is in accordance with another study which showed that flea allergens involved in flea allergy dermatitis are mostly found in flea saliva [24]. The fact that flea saliva only represents 0.5% of the proteins in whole-body flea extracts might somehow explain why intradermal skin testing with whole-body flea extracts has been associated with variable results [24]. In the same study, rCte f1 was also used as a reagent for intradermal skin testing and the results were not as accurate as for pure flea saliva: sensitivity was 40% and specificity 90% [7]. Pure flea saliva and rCte f1 are not commercially available for skin testing.

In vitro tests

Serological tests

The use of serological tests for the diagnosis of flea allergy dermatitis has also been a great source of debate. Sensitivity, specificity and reproducibility vary greatly, as does the quality of flea allergens used. Whatever the technique used, delayed reactions are missed.

These tests are based on the detection by enzyme-linked immunosorbent assays (ELISA) of specific immunoglobulin IgE or IgG. IgE or IgG specific to *Ctenocephalides felis felis* in the serum of a dog suspected of FAD is detected by addition of an antiglobulin linked to an enzyme; the complex immunoglobulin/antiglobulin/enzyme is then detected and measured by addition of the enzyme substrate [26]. In the case of IgE, this system has to be very sensitive because of the small concentration of IgE in serum [20]. Results of different studies using these serological tests vary considerably: some authors have found high levels of IgE or IgG in flea-allergic dogs when compared with normal dogs [27] whereas others have found the opposite [24, 28].

One of the most recent assays uses the high affinity Fc epsilon receptor (FcεRIα) to detect anti-flea saliva IgE in canine sera. This test has an excellent specificity whereas sensitivity is improved by the use of highly purified flea salivary antigens and rCte f1. In one study, when results of this test were compared to those of intradermal skin testing with pure flea saliva in clinical cases of flea allergy artificially sensitised dogs, and dogs never exposed to fleas, the test was found to be reliable for FAD diagnosis (sensitivity 78%; specificity 91% and accuracy 88%) [29]. In another independent study, results of this *in vitro* test were compared to a clinical approach to FAD diagnosis based on history, clinical signs and response to strict flea control. Sensitivity of the test was 87%, specificity 53% and accuracy 64% [7].

Cellular tests

Only direct activation of canine basophils has been used with flea extracts. In this test, basophil degranulation is provoked by contact with the offending allergen, in this case coming from a flea extract. When results of this assay are compared with those of intradermal skin testing with flea extracts, sensitivity and specificity were 80%. However, the diagnostic value of these tests for the diagnosis of FAD has not yet been established [21].

Response to flea control

In the face of poor reliability of allergy testing with commercially available flea assays, response to strict flea control can be used to confirm flea allergy dermatitis. Trial flea control should involve the flea-allergic dog, all in-contact animals and their environment. The aim is to kill adult fleas on affected animals, to eliminate fleas acquired from infested premises and to prevent re-infestation. Effective residual insecticides are nowadays available to kill adult fleas, and insect growth regulators should be used to disrupt the flea life cycle. A permethrin-pyriproxyfen spray has been found to be a useful product for performing a therapeutic trial to confirm a diagnosis of flea allergy dermatitis in dogs [30].

Mechanical control procedures (vacuuming, cleaning, possibly removing all furniture or materials the pets are in contact with) and preventing other animals that can carry fleas from entering resting areas of pets are also important. Cats that wander in and out are a frequent cause of treatment failure [8].

Trial flea control is not always reliable in FAD diagnosis because it must take into account the level of flea challenge and the level of "allergenic threshold" for that individual dog. It is essential for the clinician to be aware of efficacy, frequency of administration, dosage and mode of action of flea control products. In the study with the permethrin-pyriproxyfen spray, flea control was applied weekly on the flea allergic dogs only (no flea control on the in-contact animals or in the environment was performed) for 3 times. This extra-label use led to a reduction in lesional and pruritus scores of more than 75% in all of these dogs. No side-effects were observed [30]. Strict owner compliance is necessary both at the outset of flea control measures and also throughout their duration. [14]. Even with adequate flea control, clinical improvement can take a long time (4 to 8 weeks) [31, 32].

No anti-pruritic drug should be used during the trial. This can be a problem in dogs that show slow clinical improvement. When secondary infections are present, they must be cleared but treatment required in these cases makes interpretation of the trial difficult.

Conclusion

Diagnosis of canine flea allergy dermatitis relies on a thorough history and physical examination, eliminating other differential dermatoses, providing appropriate flea control for the flea-allergic dog, all in-contact animals and their environment. Clinical signs and lesion distribution are strongly suggestive of the diagnosis. Dorsolumbar lesions and pruritus have been found, in many cases, to be discriminating criteria . However, this is not sufficient for a definitive diagnosis. Demonstration of fleas is not always possible in flea allergic dogs and appropriate flea control is often difficult both to initiate and maintain. Some in-vivo and in-vitro allergy tests can be used to document sensitisation to flea allergens in flea-allergic dogs but their use is controversial. A definitive diagnosis of flea allergy in the dog is made by pooling evidence from different sources.

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