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Atopic dermatitis in dogs – Part 1 Diagnosis

Atopic dermatitis is a common, pruritic, allergic skin disease in dogs. A hereditary predisposition has been described although an interaction of dog and environmental factors is considered important.

Labrador retrievers, West Highland White Terriers, English Setters, Boxers, Yorkshire Terriers and Bulldogs are among breeds thought to be predisposed. Age of onset is typically between 6 months and 3 years and there is no gender predilection. Secondary bacterial and yeast infections are common.

Diagnosis is based on history, clinical signs and elimination of differentials. Allergy testing is used to identify allergens for immunotherapy. Signs may wax and wane but frequently worsen with age.

Key words: Pruritus, dog, allergy, skin, atopy

Introduction

Atopic dermatitis is a genetically predisposed, inflammatory and pruritic, allergic skin disease with characteristic clinical features associated with IgE, most commonly directed against environmental allergens (Halliwell, 2006).

It is believed to occur commonly in dogs though its true incidence in the general canine population is unknown (Hillier and Griffin, 2001). In one survey conducted in general practices in the UK (Hill et al, 2006), atopic dermatitis was diagnosed in 4.8% of 559 dogs with skin problems. However, in this survey, diagnosis was often incomplete (e.g. otitis, pyoderma, allergy) or not determined. The incidence of atopic dermatitis in 280 dogs referred with a dermatological problem to Re-Fur-All Referrals in southern England

over 18 months in 2002 and 2003, was approximately 78% (Craig, unpublished observations; Fig. 1), of which 85-90% were sensitive to house dust mites and/or forage (storage) mites (Fig. 2).

Pathogenesis

A hereditary predisposition to developing atopic dermatitis has been described (Shaw et al, 2004) but not linked to any one gene. An interaction of dog and environmental factors is considered important. Dog factors include impaired skin barrier function (Marsella et al, 2011), immunological aberrations and altered profiles of inflammatory mediators (Miller et al, 2013). Reactivity to house dust mites, forage mites, pollens, epithelia and other environmental allergens is thought to play an important role but IgE

Incidence of atopic dermatitis at Re-Fur-All Referrals (2002-2003) n=280

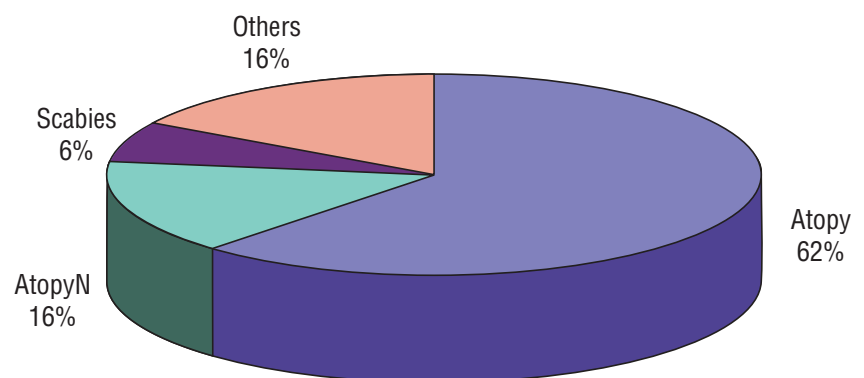


Figure 1: incidence of atopic dermatitis in dogs referred to Re-Fur-All Referrals.

- Atopy = dogs with consistent history and clinical signs, and positive intradermal and/or serological test.
- AtopyN = dogs with consistent history and clinical signs but no positive reaction demonstrated on either intradermal or serological test.



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production does not always lead to clinical disease, and development of clinical disease cannot be predicted from IgE level (DeBoer and Hill, 1999). The inhalation route was once thought to be the principal source of allergen exposure but recent studies suggest that all routes, especially the epicutaneous route may be involved (Marsella et al, 2006).

Forage mites have been found in unopened commercial dry dog foods (Brazis et al, 2008), and ingestion of forage mite allergens has been shown to trigger a dermatitis clinically indistinguishable from atopic dermatitis, in laboratory Beagles (Marsella and Creary, 2007). The extent to which atopy and cutaneous adverse food reaction are separate conditions is contentious but many dermatologists believe that foods can trigger flares in atopic dogs.

Antigens of the yeast, *Malassezia pachydermatis*, can trigger hypersensitivity reactions in atopic dogs (Bond et al, 2002) (Fig. 3). Various studies have suggested that *Staphylococcus pseudintermedius* might behave as an allergen in some dogs and elicit an IgE response (Morales et al, 1994). However, a cutaneous, immediate hypersensitivity reaction to staphylococcal antigens has not been conclusively documented in dogs (Miller et al, 2013).

Other factors proposed include season of birth, maternal diet and probiotics (Marsella and Creary, 2007). One study found no effect of gender, environment, vaccination, season of birth or worming routine on the likelihood of developing atopic dermatitis but did demonstrate a lower incidence of atopic dermatitis in puppies from bitches fed homemade, non-commercial diets (Nodtvedt et al, 2007).

Clinical signs

Dogs typically show initial signs between the age of 6 months and 3 years (Griffin and DeBoer, 2001). Signs may be seasonal or non-seasonal from the outset. All breeds are susceptible but some are thought to be more at risk. Precisely which ones varies with geographical location and gene pool but Labrador Retrievers (Fig. 4), English Setters, West Highland White Terriers, Boxers, English Bulldogs and Yorkshire Terriers are among the breeds thought to be more at risk in the UK, Europe and the USA (Nuttall et al, 2009). No gender predilection has been proved.

Pruritus, often intermittent and variable in severity, is the main feature, typically



Figure 2: *Dermotophagoides pteronyssinus*, house dust mite.

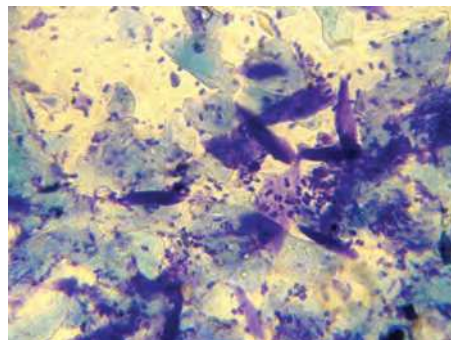


Figure 3: Antigens of the yeast, *Malassezia pachydermatis*, can trigger hypersensitivity reactions in atopic dogs



Figure 4: Papules, pustules, alopecia, excoriation, hyperpigmentation and skin thickening in a 1-year old, spayed female Labrador Retriever, a breed predisposed to atopic dermatitis

affecting the face and ears, feet, axillae and inguinal regions (Fig. 5). Erythema is often primary but pruritus and secondary microbial infection, most commonly with either or both *Staphylococcus pseudintermedius* and *Malassezia pachydermatis* (Fig. 6), can lead to self-trauma, excoriation, alopecia, salivary staining, papulo-pustular dermatitis, crusting, scaling, ulceration, hyperpigmentation, lichenification, acute moist dermatitis, acral lick dermatitis (Fig. 7) and fibro-pruritic nodules. Otitis externa (Fig. 8) and conjunctivitis are common. All signs of atopic dermatitis are very variable.



Figure 5: Erythema, alopecia, hyperpigmentation and skin thickening in a 5 year old neutered male West Highland White Terrier, a breed predisposed to atopic dermatitis



Figure 6: *Malassezia dermatitis* in an atopic West Highland White Terrier



Figure 7: Acral lick dermatitis on the distal limb of an atopic Labrador Retriever



Figure 8: Otitis externa in a West Highland White Terrier with chronic atopic dermatitis

Diagnosis

The diagnosis is based on history, clinical signs and exclusion of other causes of pruritus. The differential diagnosis includes flea allergic dermatitis, cutaneous adverse food reaction, ectoparasitic infestations (e.g. sarcoptic mange, cheyletiellosis, pediculosis and harvest mite infestation), bacterial folliculitis, *Malassezia* dermatitis, and cutaneous drug reaction. There is no definitive test but skin scrapings, coat brushings, hair plucks, tape strips for cytology and fungal culture may be indicated in the initial investigation to rule out differentials. Skin biopsies are usually unnecessary but histopathology typically reveals a superficial perivascular, spongiotic dermatitis.

Allergy testing is indicated to demonstrate allergen-specific IgE in either skin or serum, and to select specific allergens for immunotherapy; not to make a diagnosis of atopic dermatitis. Allergens considered important include house dust mites (*Dermatophagoides* spp.), forage mites (e.g. *Acarus*, *Lepidoglyphus* and *Tyrophagus*), animal and bird epithelia, pollens, insects (e.g. *Ctenocephalides*, *Tabanus* and *Musca*) and moulds. Testing, both intradermal and serological, for food allergens is unreliable (Miller et al, 2013).

Intradermal testing (Fig. 9) is used to demonstrate cutaneous allergen-specific IgE. It involves the intradermal injection of 0.05 ml of aqueous allergen test extracts, alongside a positive (1:100,000 histamine phosphate) and a negative (saline) control. Use of an appropriate sedative to minimise stress is recommended. Medetomidine, thought not to interfere with intradermal test reliability, is commonly given, followed by atipamezole as a reversing agent. After 15 minutes, the mean diameter of resulting wheals is measured. A positive reaction is indicated when wheal diameter is larger than the mean diameter of the two controls. Both objective measurement and subjective assessment of wheal depth and degree of erythema are conducted.

Meaningful interpretation requires considerable experience. Skin test reaction size does not necessarily correlate with severity of clinical signs. Reactions typically reach their peak within 15 minutes but delayed reactions may occur up to 48 hours later. False negative (Table 1) and false positive (Table 2) reactions can occur. One of the most common potential causes of false negative results is drug administration. This has not been extensively researched but glucocorticoids, antihistamines, and certain sedatives and anaesthetics (e.g.

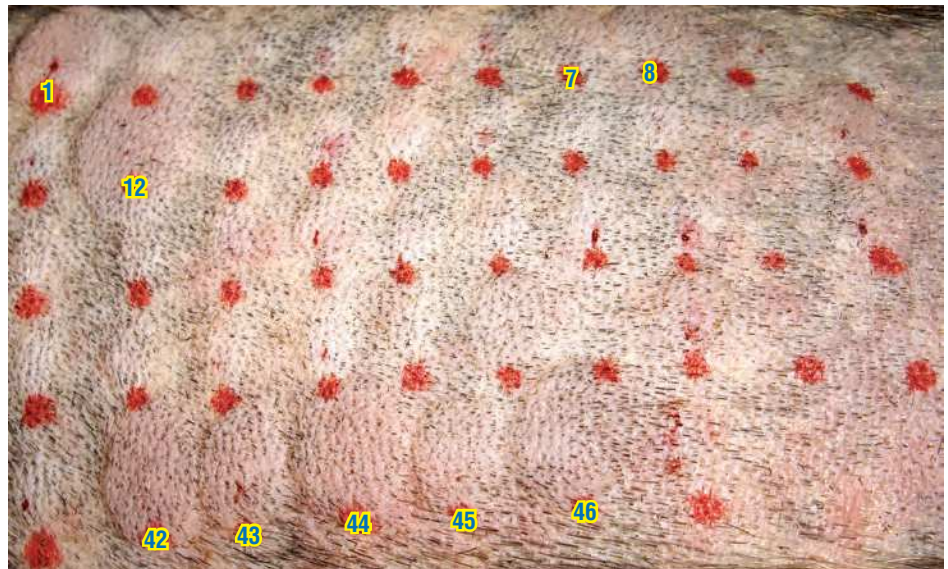


Figure 9: Intradermal testing on the left flank of a 2-year old cross-breed dog. Note prominent, erythematous wheals around injection sites 1 (positive control), 7,8,12, 42-46 (numbered horizontally from top left). The negative control, saline is adjacent to the positive control, histamine (1).

Table 1: Possible reasons for false-negative intradermal test reactions

Subcutaneous injection of extract
Inadequate amount of extract injected
Drug interference: glucocorticoid, antihistamine, ACP, progesterone compound
Testing during oestrus or pseudopregnancy
Stress

Table 2: Possible reasons for false-positive intradermal test reactions

Irritant effect of allergen test extract
Contamination of extract
Poor injection technique
Dermatographism (a wheal and flare reaction provoked by pressure)

Table 3: Proposed optimal withdrawal times for various drugs prior to intradermal testing based on review of evidence prior to 2012 (Olivry et al, 2013)

Drug	Intradermal test
Glucocorticoid	
- Topical	2 weeks
- Oral	2 weeks
- Long-acting injection	unknown
Antihistamine - Oral	1 week

acepromazine, diazepam, propofol and ketamine) have been found to reduce intradermal test reactivity (Hillier and DeBoer, 2001).

The factors influencing drug withdrawal times for allergy testing in dogs are highly complex but authors of a recent review of studies conducted prior to 2012 (Olivry, 2013) proposed optimum withdrawal times for certain drugs (Table 3). There was no evidence to recommend a withdrawal period for ciclosporin, essential fatty acids or ketoconazole. One study has shown no effect of oclacitinib (Zoetis UK Limited) on sensitivity to intradermal house dust mite injection in 24 dogs experimentally sensitised to house dust mites (Aleo et al, 2013).

Serological testing, now widely available, is used to detect circulating levels of allergen-specific IgE. Measurement of total IgE is a poor indicator of clinical allergy and even allergen-specific IgE can have poor specificity and low positive predictive value (Bond et al, 1994). Positive serological test results do not necessarily correlate with either clinical manifestations of allergy or with intradermal test results (DeBoer and Hillier, 2001). One advantage of serological testing over intradermal testing is that results are considered less likely to be influenced by prior or current drug therapy (Miller et al, 2013). Few data are available on the effects of drug administration on serology test results (Olivry, 2013) although one recent study demonstrated no significant changes in dust mite IgE titres following 14 days treatment with either oclacitinib (0.4 mg/kg BID) or prednisolone (0.5 mg/kg BID) (Aleo et al, 2013).

Prognosis

Dogs with atopic dermatitis will always be susceptible to episodes of variable, intermittent pruritus and other clinical signs as outlined above. Signs may worsen with age (Miller et al, 2013).

Summary

Atopic dermatitis is a common, pruritic, allergic skin disease in dogs. Treatment of this challenging condition will be discussed in the next issue of Vet CPD.

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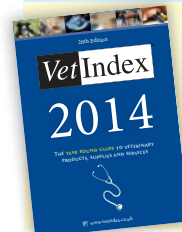
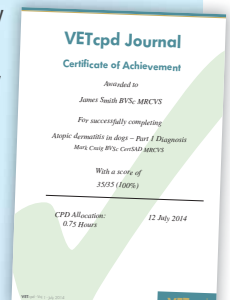
1. Which of the following is currently believed to be the most accurate definition of atopic dermatitis?

- A) A congenital disease with characteristic clinical features associated with elevated IgG production to environmental allergens.
- B) A congenital disease with characteristic clinical features associated with elevated IgE production to environmental and food allergens.
- C) A genetically predisposed, inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE most commonly directed against environmental allergens.
- D) A genetically predisposed, inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgA most commonly directed against environmental allergens.
- E) A hereditary predisposition to develop hypersensitivity to environmental allergens.

2. Which route(s) of allergen exposure is/are thought to be involved in the pathogenesis of atopic dermatitis?

- A) Oral route only
- B) Inhalation and oral route only
- C) Epicutaneous route only
- D) All routes especially inhalation
- E) All routes especially epicutaneous

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