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Atopic dermatitis in dogs – Part 2 Therapeutics

Canine atopic dermatitis is a common pruritic skin condition. Therapy needs to be customised to the individual patient and involves the identification and avoidance of flare factors, improvement of skin and coat condition, reduction of pruritus and skin lesions, and preventing recurrence of clinical signs.

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

Introduction

Canine atopic dermatitis (CAD) is a complex, chronic, relapsing, pruritic skin condition, the management of which often involves many interventions. Individuals can tolerate some pruritogenic stimulus without becoming pruritic but if stimuli exceed a certain level (the pruritic threshold), pruritus ensues (Fig 1). Treatment needs to be customised and aimed at reducing pruritic stimuli below the patient's pruritic threshold. Therapy involves the identification and avoidance of flare factors, improvement of skin and coat condition, reduction of pruritus and skin lesions, and preventing recurrence of clinical signs (Table 1).

Identification and avoidance of flare factors

Avoidance of incriminated allergens

Where allergens have been incriminated from food trials, flea control, owner observation, history taking and allergy testing (intradermal or serology), avoidance of these allergens should be attempted (Olivry et al, 2010), with a view to reducing the need for pharmacotherapy with all its inherent risks and uncertainties. Well-conducted ectoparasite control programmes and the feeding of carefully selected diets are feasible and can be helpful but avoidance of common environmental allergens (e.g. house dust mites and pollens) is usually impractical or even impossible for most dogs and their owners.

Acaricides; impermeable, hypoallergenic mattress covers; removal of carpets and upholstered furniture; controlling indoor temperature and humidity; steam cleaning; frequent washing and vacuuming of the environment (Fig. 2A); and external kennelling (Fig 2B) are commonly advised although little is known regarding their efficacy in either

reducing household allergen levels or providing clinical benefit for dogs with CAD. One uncontrolled study (Swinnen and Vroom, 2004) reported that spraying the household environment with a product containing benzyl benzoate was effective in eliminating guanine, a major component of house dust mite excrement. The authors concluded that house dust mite elimination was a useful tool in the management of house dust mite-sensitive dogs and that treatment with benzyl benzoate was as effective as allergen-specific immunotherapy.

Flea control

Exposure to fleas should be assessed in every case and an effective flea control programme established.

Antimicrobial therapy

Systemic antibiotics effective against *Staphylococcus pseudintermedius* should be given at an appropriate dose and for a suitable duration to treat episodes of pyoderma (Fig. 3). Topical antimicrobial agents commonly used in canine skin infections include chlorhexidine, povidone-iodine, ethyl lactate, and benzoyl peroxide. A shampoo containing chlorhexidine and miconazole (Malaseb, Dechra Veterinary Products Ltd) is normally a very effective anti-yeast treatment (Figs 4, 5). Oral ketoconazole (Nizoral, Janssen, 5–10 mg/kg BID for 3 weeks) may sometimes be indicated to treat *Malassezia* dermatitis but systemic therapy is usually unnecessary.

Improvement of skin and coat

Topical therapy

Topical therapy provides many benefits for atopic dogs, often reducing or even eliminating the need for systemic therapy (Loeffler et al, 2007). Washing with an appropriate, non-irritating shampoo can reduce the level of allergen in the coat and the amount penetrating the skin. It



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Figure 1: Erythema, alopecia, excoriation in a dog with atopic dermatitis.



Figure 2A: Frequent household vacuuming is commonly advised for dogs with house dust mite allergy.



Photo: courtesy of Claire Jarvis, Pool House Veterinary Hospital.

Figure 2B: External kennelling may be helpful in dogs sensitive only to indoor allergens such as house dust mites.

can also improve skin barrier function and help resolve and prevent secondary infection (Fig 6). These actions may, in themselves, help to reduce pruritus, but colloidal oatmeal and other ingredients, considered anti-pruritic, are often included in shampoos to enhance this effect. Shampoos are often followed by a rinse to be left on the body for maximal residual benefit, or a conditioner that is rinsed off. One oil-free skin and coat conditioner containing water, glycerin, lactic acid, urea, propylene glycol, benzalkonium chloride, and benzaldehyde (Humilac, Virbac Animal Health) can be sprayed directly onto the skin and coat or applied as an after-shampoo rinse.

Spot-on products are now also available for improving epidermal barrier function in atopic dogs. One product (Allerderm Spot-on, Virbac Animal Health) contains

Table 1: Management of acute and chronic canine atopic dermatitis, based on recommendations by the International Task Force on Canine Atopic Dermatitis (Olivry et al, 2010)

General strategies	Specific measures for acute flares	Additional measures to be considered for chronic CAD
Identification and avoidance of flare factors e.g. fleas, food items and environmental allergens such as house dust mites and pollens e.g. skin and ear infections with <i>S. pseudintermedius</i> or <i>M. pachydermatis</i>	Flea control, restricted diet, environmental restriction and household cleaning strategies Topical and/or systemic antimicrobials	
Improvement of skin and coat	Non-irritating shampoo	Conditioners and rinses EFA supplementation Topical lipids*
Reduction of pruritus and skin lesions with pharmacological agents	Topical glucocorticoid Short course of oral glucocorticoid. Oclacitinib*	Oral cyclosporin
Preventing recurrence of signs		Allergen-specific immunotherapy

* Not in original recommendations by Olivry et al



Figure 3: Abdominal erythema and papules in a dog with superficial pyoderma.



Figure 4: Ventral abdominal and inguinal erythema and hyperpigmentation in a Basset with *Malassezia* dermatitis.

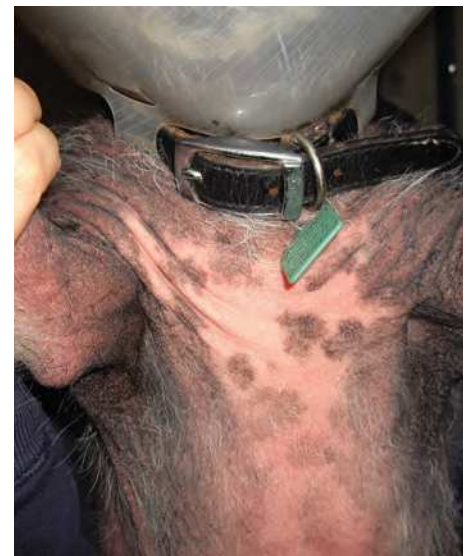


Figure 5: Chlorhexidine and miconazole is normally a very effective combination for controlling yeasts in dogs with atopic dermatitis.



Figure 6: Washing with an appropriate shampoo provides many benefits for dogs with skin disorders.

Photo: courtesy of Vickie Boswell, Milton Keynes Veterinary Group

a mixture of ceramides, fatty acids and cholesterol. Ceramides form a major component of the lipid bilayer in the stratum corneum and appear to be important in controlling water loss from the epidermis (Miller, Griffin and Campbell, 2013). Initially, the product is applied once weekly for 4 weeks and subsequently once a month. For best results, manufacturers advise applying after a bath when the fur is completely dry.

Essential fatty acids (EFAs)

Omega 3 and omega 6 essential fatty acids have been used to manage pruritus and inflammation in dogs with CAD. Supplements can change plasma and skin fatty acid levels but this does not always correlate with clinical improvement (Mueller et al, 2004). EFA supplementation might also modulate clinical signs associated with abnormal skin barrier function (Olivry et al, 2001).

Reduction of pruritus and skin lesions: Anti-inflammatory therapy (AIT)

AIT may be warranted if allergen avoidance is impractical or inadequate in controlling clinical signs.

Glucocorticoids

These drugs are mostly very effective in relieving pruritus in atopic dogs. They are also cheap and easy to administer. Unfortunately, the risk of acute and chronic side-effects associated with systemic glucocorticoid therapy is considerable (Olivry and Sousa, 2001; Miller et al, 2013).

Topical: Topical administration allows direct application of the glucocorticoid to the site of inflammation and may reduce the need for systemic therapy. However, long-term use has been associated with cutaneous atrophy and sub-epidermal vesiculation (Gross et al, 1997). Hydrocortisone aceponate (Cortavance, Virbac), licensed in the UK for short-term, symptomatic treatment of inflammatory and pruritic dermatoses in dogs, has been found to be effective and well-tolerated (Nuttall et al, 2009) with minimal systemic absorption. A gel containing fusidic acid and betamethasone (Fuciderm, Dechra Veterinary Products) is licensed for the treatment of surface pyoderma.

Systemic: Oral administration is preferred because the dose can be more precisely

Table 2: Treatment of CAD with systemic antipruritic agents

Drug	Trade name	Induction dose /day
Glucocorticoid		
Prednisolone	Prednidale (Dechra Veterinary Products Ltd)	0.5 mg/kg SID or BID
Methylprednisolone	Medrone V (Zoetis UK Ltd)	0.4 mg/kg SID or BID
Antihistamine		
Chlorpheniramine	Piriton*	0.4 mg/kg TID
Clemastine	Tavegil*	0.05-0.1 mg/kg BID
Diphenhydramine	Nytol*	1-2 mg/kg TID
Hydroxyzine	Ucerax*, Atarax*	2 mg/kg BID or TID
Cyclosporin	Atopica (Novartis Animal Health UK Ltd)	5 mg/kg SID for 4 weeks
Oclacitinib	Apoquel (Zoetis UK Ltd)	0.4-0.6 mg/kg BID for 2 weeks

* Unlicensed for use in dogs in UK

regulated and the drug withdrawn at any time. Oral glucocorticoids are very effective in the treatment of CAD (Olivry et al, 2010) leading to rapid reduction or elimination of pruritus when given at an appropriate dose (Table 2). Ideally, they should be given only when other less risky forms of therapy are inadequate, and for a maximum period of 3 months (Miller et al, 2013). Once pruritus has been controlled, the dose should be tapered to the lowest possible alternate day level. Some dogs may cope with less frequent dosing. Therapy needs to be customised for each patient balancing satisfactory control with minimising side-effects.

Cyclosporin

Cyclosporin (Atopica, Novartis Animal Health), a polypeptide metabolite of the fungus *Tolypocladium inflatum*, has been found to be an effective treatment for CAD, comparable to (methyl) prednisolone (Olivry and Mueller, 2003). It is believed to inhibit cytokine-induced activation of certain cells that initiate the cutaneous immune response and others that mediate allergic reactions (Steffan et al, 2006). The onset of satisfactory clinical benefit may take 4-6 weeks (Olivry et al, 2010). A starting dose of 5 mg/kg/d (Table 2) is therefore given for at least a month. Once clinical signs are controlled, alternate-day dosing may be adopted. Cyclosporin should ideally be given on an empty stomach (Miller et al, 2013) to optimise absorption, but can be given with food. Vomiting and diarrhoea are the most common side-effects reported (Steffan et al, 2006).

Oclacitinib

Oclacitinib (Apoquel, Zoetis UK Limited) inhibits Janus kinases (principally JAK1), enzymes that communicate signals between cell surface receptors and the nucleus (DeBoer, 2013), and inhibits the function of a variety of pro-inflammatory, pro-allergic and pruritogenic cytokines dependent on Janus kinase activity (Cosgrove et al, 2013). It is licensed in the UK for treatment of CAD. A dose of 0.4-0.6 mg/kg twice daily for two weeks is recommended before reducing to once daily dosing. Its anti-pruritic effects are rapid in onset and may be accompanied by anti-inflammatory actions (Gonzales et al, 2013). It appears to be well tolerated at least in the short-term. In two studies, the frequency and type of abnormal health events were similar for the oclacitinib – and placebo-treated dogs and included GI disturbances, anorexia, lethargy, subcutaneous nodules and polydipsia.

Antihistamines

Antihistamines (Table 2) are commonly prescribed for atopic dogs although no conclusive evidence of efficacy has been demonstrated (Olivry et al, 2010). Therapy with chlorpheniramine, clemastine and hydroxyzine may be attempted, each for 1-2 weeks before deciding on efficacy. Antihistamines may be more effective at minimising pruritus once pyoderma, *Malassezia* dermatitis and more severe irritation have been addressed by other means. When combined with other treatments such as EFA supplementation, they may help to reduce steroid requirement.

Allergen-specific immunotherapy (ASIT)

ASIT involves giving increasing quantities of an allergen extract to an allergic patient to improve signs associated with subsequent exposure to the causative allergen (Bousquet et al, 1998; Olivry et al, 2001). The precise mechanisms of ASIT are unknown but thought to involve induction of T regulatory cells, and alteration of antibody production, cytokine secretion and mast cell degranulation (Miller et al, 2013).

Immunotherapy protocols vary considerably in relation to the form of allergen used (aqueous or alum-precipitated), number and frequency of injections in induction phase, dose, potency of extract, and route of administration. ASIT is most commonly administered by subcutaneous injection but sublingual immunotherapy is also available. A number of ASIT products are available, none specifically licensed in the UK. Artuvetrin (ALK), the only product licensed within the EU, has a full product licence in the Netherlands. The maintenance dose for Artuvetrin alum-precipitated ASIT is typically given monthly but can be administered every 2-3 weeks or every 5-6 weeks according to clinical need.

The efficacy of ASIT is very difficult to assess clinically in any one patient, and months of therapy may be required for benefit to occur. Many open studies have demonstrated good success rates (Loewenstein and Mueller, 2009) and in the only prospective, double-blind, placebo-controlled trial, 59% of dogs treated with ASIT and 21% of dogs with placebo showed a greater than 51% improvement in clinical signs (Willemse et al, 1984). However, one recent review concluded there was a paucity of scientific trials to determine the true efficacy of ASIT in dogs and the optimal allergen doses and frequency of injections (Loewenstein and Mueller, 2009). The most common adverse reaction reported is increased pruritus, systemic reactions (e.g. weakness, depression, anxiety, panting, hyperactivity, vomiting, diarrhoea, urticaria, collapse and anaphylaxis) being reported in about 1% of dogs (Walton Angarano and MacDonald, 1991).

Patient selection is important: ASIT is indicated in CAD when intradermal testing or allergen-specific serology has enabled identification of allergens, when allergen contact is unavoidable, and when symptomatic therapy is

ineffective, impractical or associated with unacceptable side-effects (Griffin and Hillier, 2001). Although results appear to be independent of whether allergen selection is based on intradermal or serological testing, one study has suggested slightly better results if both procedures are considered (Anderson and Sousa, 1992). Reports, mostly from anecdotal studies, are conflicting about the effects on clinical outcome, of age (at disease onset and at start of ASIT), breed, gender, duration and seasonality of disease, and the number and type (e.g. pollens versus house dust mites) of allergens to which the patient is hypersensitive (Loewenstein and Mueller, 2009).

Owners must be fully informed about the procedures, understand the limitations and possible adverse reactions, be able to present the patient for regular monitoring, and be prepared to continue therapy for at least a year before deciding on its long-term efficacy (Miller et al, 2013). ASIT is not curative and therefore, life-long therapy is typically recommended. Dogs that are unruly or hate coming to the vets may be unsuitable although many owners are happy to administer the product at home.

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Conclusion

Canine atopic dermatitis is a common pruritic skin condition. Therapy needs to be customised to the individual patient and involves the identification and avoidance of flare factors, improvement of skin and coat condition, reduction of pruritus and skin lesions, and preventing recurrence of clinical signs.

References

- Anderson RK, Sousa CA (1992) In vivo vs in vitro testing for canine atopy, In: *Advances in Veterinary Dermatology*, Pergamon Press, 425
- Bousquet J, Lockey R, Malling HJ et al (1998) Allergen immunotherapy: therapeutic vaccines for allergic diseases. World Health Organisation. *American Academy of Allergy, Asthma and Immunology. Annals of Allergy, Asthma and Immunology* 81, 401-405
- Cosgrove SB, Wren JA, Cleaver DM, Martin DD, Walsh KF, Harfst JA, Follis SL, King VL, Boucher JF, Stegemann MR (2013) Efficacy and safety of oclacitinib for the control of pruritus and associated skin lesions in dogs with canine allergic dermatitis. *Veterinary Dermatology* 24, 479-487
- Cosgrove SB, Wren JA, Cleaver DM, Walsh KF, Follis SL, King VL, Tena JK, Stegemann MR (2013) A blinded, randomized, placebo-controlled trial of the efficacy and safety of the Janus kinase inhibitor oclacitinib (Apoquel) in client-owned dogs with atopic dermatitis. *Veterinary Dermatology* 24, 587-597
- DeBoer DJ (2013) What's new? Systemic therapy for atopic dermatitis. In: *proceedings of British Veterinary Dermatology Study Group, Autumn meeting, November 2013*, 61-63
- Gonzales AJ, Bowman J, Fici G, Zhang M, Mann DW (2013) Oclacitinib (Apoquel; Zoetis) is a novel Janus kinase inhibitor that has activity against canine pro-allergic and pro-inflammatory cytokines. *Veterinary Dermatology* 24, 384-385
- Griffin CE, Hillier A (2001) The ACVD task force on canine atopic dermatitis (XXIV): allergen-specific immunotherapy. *Veterinary Immunology and Immunopathology* 81, 363-383
- Gross TL, Walder EJ, Ihrke PJ (1997) Subepidermal bullous dermatosis due to topical corticosteroid therapy in dogs. *Veterinary Dermatology* 8, 121-131
- Loeffler A, Baines S, and Toleman, M et al (2008) In-vitro activity of fusidic acid and mupirocin against coagulase positive staphylococci from pets *Journal of antimicrobial chemotherapy*, 62, 1301-1304
- Loewenstein C and Mueller RS (2009) A review of allergen-specific immunotherapy in human and veterinary medicine. *Veterinary Dermatology* 20, 2, 84-98
- Miller WH, Griffin CE, Campbell KL (2013). In: Muller and Kirk's *Small Animal Dermatology* 7th ed. Elsevier pp 141, 147, 150-152, 383
- Mueller R, Fettman MJ, Richardson K. et al (2004). The effect of omega 3 fatty acid supplementation on cutaneous and plasma fatty acid concentrations in dogs with atopic dermatitis. *Veterinary Dermatology* 15s, 65
- Nuttall T, Mueller R, Bensignor E, Verde M, Noli C, Schmidt V, Rème C. Efficacy of a 0.0584% hydrocortisone aceponate spray in the management of canine atopic dermatitis: a randomised, double blind, placebo-controlled trial. *Veterinary Dermatology* 20, 191-198
- Olivry T, DeBoer DJ, Favrot C, Jackson HA, Mueller RS, Nuttall T, Prélard P. (2010). Treatment of canine atopic dermatitis: 2010 practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21, 233-248
- Olivry T, DeBoer DJ, Griffin CE et al (2001). The ACVD task force on canine atopic dermatitis (XXIV): allergen-specific immunotherapy. *Veterinary Immunology and Immunopathology* 81, 363-383
- Olivry T, Foster AP, Mueller RS, McEwan NA, Chesney C, Williams HC (2010). Interventions for atopic dermatitis in dogs: a systematic review of randomised controlled trials. *Veterinary Dermatology* 21, 4-22
- Olivry T, Marsella R, Hillier A (2001). The ACVD task force on canine atopic dermatitis (XXIII): are essential fatty acids effective. *Veterinary Immunology and Immunopathology* 81, 347-362
- Olivry T, Mueller RS (2003). Evidence-based veterinary dermatology: a systematic review of the pharmacotherapy of canine atopic dermatitis. *Veterinary Dermatology* 14, 121-146
- Olivry T, Sousa CA (2001). The ACVD task force on canine atopic dermatitis (XIX): general principles of therapy. *Veterinary Immunology and Immunopathology* 81, 311-316
- Olivry T, Sousa CA (2001). The ACVD task force on canine atopic dermatitis (XX): glucocorticoid pharmacotherapy. *Veterinary Immunology and Immunopathology* 81, 317-322
- Steffan J, Favrot C, and Mueller R (2006) A systematic review and meta-analysis of the efficacy and safety of cyclosporin for the treatment of atopic dermatitis in dogs. *Veterinary Dermatology* 17, 3-16
- Swinen C, Vroom M (2004) The clinical effect of environmental control of house dust mites in 60 house dust mite-sensitive dogs. *Veterinary Dermatology* 15, 31-36
- Walton Angarano D and MacDonald JM (1991). Immunotherapy in canine atopy. In: Kirk RW, Bonagura JD, eds. *Current Veterinary Therapy XI*, Philadelphia, WB Saunders. 505-508
- Willemse A, Van den Brom WE and Rijnberk A (1984) Effect of hyposensitisation on atopic dermatitis in dogs. *Journal of the American Veterinary Association* 184, 1277-1280

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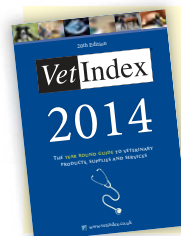
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