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Managing canine atopic dermatitis with topical therapy

Canine atopic dermatitis is a common allergic skin disease. Topical therapy can be soothing, antimicrobial, and cleansing. It can reduce or even eliminate the need for systemic therapy, thereby cutting cost, the risk of associated adverse reactions, and the likelihood of the patient developing antibiotic resistance. Although topical therapy is typically used alongside systemic therapy, it may be used as sole therapy. The aims of topical therapy are influenced by the condition of the skin and coat, the level of pruritus and the degree of microbial overgrowth. Appropriate products can be selected and customised for both patient and owner. Topical medications consist of active ingredients in a vehicle that facilitates application to the skin. Shampoos, rinses, sprays, foams, mousses and spot-ons are practical and effective ways to deliver active ingredients to large areas of skin. Gels, creams, wipes, pads and ointments are good options for less hairy regions or localised lesions.

Key words: topical, dog, shampoo, allergy, pyoderma, pruritus

Introduction

Canine atopic dermatitis (CAD) is a common allergic skin disease (Figure 1). Variable intermittent pruritus is the main clinical feature, typically affecting the face and ears, feet, axillae and inguinal regions. Bacterial and yeast overgrowths with *Staphylococcus pseudintermedius* and *Malassezia pachydermatis* are common. Affected dogs have a life-long susceptibility, and signs may worsen with age (Miller *et al.* 2013a). Although the response to systemic medication can be dramatic, topical therapy can also provide considerable benefits for dogs with CAD. Today's small animal practitioner is faced with an ever-increasing range of products for topical therapy. Whilst this provides a tremendous opportunity for improving the welfare of our dermatology patients, having such a large choice can also be bewildering.

Why use topical therapy?

Topical therapy can be soothing, antimicrobial, and cleansing. Many of today's topical therapy products also aim to improve skin barrier function, a key factor in the pathogenesis of CAD, and enrich the diversity of the skin microbiome, now considered a significant player in maintaining skin health (Hoffman 2017; Santoro *et al.* 2020). Topical therapies are applied directly to the skin and/or the coat, enabling access of active ingredients to the target organ. They can reduce or even eliminate



Figure 1: An atopic French bulldog with widespread excoriations.



Figure 2: Topical therapy alone can be effective in some dogs with bacterial folliculitis.

the need for systemic therapy, thereby cutting cost, the risk of associated adverse reactions, and the likelihood of the patient developing antibiotic resistance (Mueller *et al.* 2012). Although topical therapy is typically used alongside systemic therapy, it may be used as sole therapy (Frank and Loeffler 2012) (Figure 2).

Selecting appropriate topical therapy

The aims of topical therapy (Table 1) should first be clarified. These will be influenced by the condition of the skin and coat (Table 2), the level of pruritus and the degree of microbial overgrowth. Appropriate products can then be selected and customised for both patient and owner (Table 3). Factors affecting the suitability of a product include its active ingredients, how it is applied to the skin and coat, and its ease of use; aesthetic considerations such as how it smells and feels can determine how well it is accepted by both patient and owner. Colour may also be important for an owner, although not for the patient. The demeanour of the patient and the ability of the owner to administer treatment are also critical.

Anything applied topically may, in some individuals, cause irritation or contact dermatitis (Nuttall 2020). Any product suspected to have triggered an adverse reaction in either the patient or owner should be avoided.

Active ingredients

Topical medications consist of active ingredients in a vehicle that facilitates application to the skin (Miller *et al.* 2013b). Active ingredients can be emollient and moisturising, anti-pruritic, anti-oxidant, anti-inflammatory, antiseborrhoeic, antimicrobial, antiparasitic, astringent (drying) and immune-modulating (Craig 2014) (Figure 3). They are now also being investigated for their ability to strengthen the mechanical and immunological skin barrier and modulate the skin microbiota (Ollivier *et al.* 2019a,b).

Improving skin barrier function

Ophytrium, extracted from Mondo Grass roots, is thought to be helpful in maintaining skin barrier function (Ollivier 2019a) and limiting adhesion and biofilm formation of *Staphylococcus pseudintermedius* (Ollivier 2019b). A reduction in pruritus and improved skin condition was reported in dogs wiped with ophytrium and 3% chlorhexidine digluconate (Gatellet 2020). Ophytrium has now replaced phytosphingosine in the Douxo range of products (Ceva Animal Health Limited). Ceramides may improve epidermal barrier function in atopic dogs. They form a major component of the lipid bilayer in

Table 1: Aims of topical therapy

Antipruritic
Antimicrobial
Deodorising
Cleansing
Degreasing
Moisturising
Reduction in need for systemic therapy

Table 2: Condition of skin and coat

Greasy skin and coat
Dry skin and coat
Presence of scale and crust
Long/short coat

Table 3: Factors affecting product selection

Aims of therapy
Active ingredients of the product
Means of delivering ingredients to skin and coat (formulation)
Ease of use
Ease of lathering
Aesthetic considerations: smell, consistency, colour
Patient demeanour
The ability of the owner to carry out treatment



Figure 3: Emollient and moisturising shampoos are indicated in dogs with dry, scurfy skin.

the stratum corneum and appear to be important in controlling water loss from the epidermis (Miller *et al.* 2013c).

Colloidal oatmeal is used commonly to treat pruritus and dry skin in dogs. Extracts of colloidal oatmeal have been shown to exhibit direct anti-oxidant and anti-inflammatory activities in people (Reynertson *et al.* 2015) and may also strengthen the skin barrier (Illynska *et al.* 2016) and improve microbiome composition (Capone *et al.* 2020) (Figure 4).



Figure 4: Oatmeal shampoos can be soothing for atopic dogs and may also strengthen the skin barrier.

Antimicrobial activity

Systemic antibiotics can cause profound alterations in the canine intestinal microbiome (Suchodolski 2011) as well as being associated with toxicity and idiosyncratic adverse reactions. Although systemic antibiotics have long been considered essential in the management of canine pyoderma, seen frequently in dogs with CAD, increasing microbial resistance to antibiotics, both systemic and topical, may create a situation in which no suitable antibiotic is available for the treatment of common diseases (Lloyd, 2012). Applying an antibacterial agent topically can result in higher drug levels at the target site than those resulting from systemic administration, and may even overcome apparent in-vitro resistance (Loeffler *et al.* 2008).

In cases of pyoderma associated with methicillin-resistant *Staphylococcus pseudintermedius* (MRSP), topical therapy is considered essential by some dermatologists (Griffin 2011) and may need to be used as sole therapy (Loeffler *et al.* 2011). Good hygiene and topical antiseptic solutions to decolonise persistent carriers of drug-resistant staphylococci is preferable to using antibiotics (Weese *et al.* 2007).



Figure 5: Washing with an appropriate shampoo provides many benefits for dogs with skin disorders (courtesy of Vickie Boswell, Milton Keynes Veterinary Group).

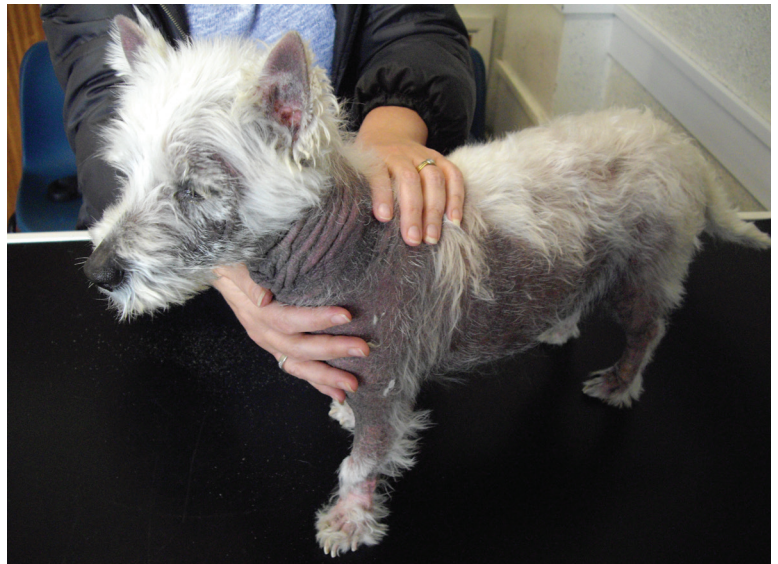


Figure 6: *Malassezia* dermatitis typically responds well to washing with chlorhexidine shampoos.

Topical antimicrobial agents commonly used in canine skin infections include chlorhexidine, povidone-iodine, ethyl lactate, fusidic acid, hydrogen peroxide, benzoyl peroxide, and miconazole. In one study, 6 out of 12 dogs with multiresistant *S. pseudintermedius* were treated successfully with topical antimicrobial therapy alone (fusidic acid, chlorhexidine, chlorhexidine and miconazole, or ethyl lactate) (Loeffler *et al.* 2007). Chlorhexidine has been shown in-vitro to be more effective for both MRSP and methicillin-sensitive *Staphylococcus pseudintermedius* (MSSP) than benzoyl peroxide, ethyl lactate, chloroxylenol and acetic acid-boric acid (Young *et al.* 2012). Chlorhexidine digluconate shampoos, foams and mousses, sprays, wipes, pads, and spot gels are available in the UK.

Some products contain a combination of antimicrobial agents such as antimicrobial peptides and substances aimed specifically at maintaining or strengthening the skin barrier. Antimicrobial peptides (AMPs) are being investigated for their ability to overcome antibiotic resistance, and rapid, broad-spectrum antimicrobial activity has been reported (Cabassi *et al.* 2013; Romani *et al.* 2013; Ghibauda *et al.* 2016; Cabassi *et al.* 2017; Jarosiewicz 2020). AMPs are available in shampoo, foam and ear flush formulations, alongside chlorhexidine digluconate and trisEDTA. Antimicrobial activity has also been claimed for topical agents such as honey (Cremers *et al.* 2020), coconut oil (Kabara, Swieczkowski, Conley *et al.* 1972; Varma *et al.* 2019), tea tree oil (Halcon and Milkus 2004), manuka oil (Song *et al.* 2020), an extract of edible plants referred to as W16P576 (Bäumer 2020), aloe vera

(Shelton 1991; Kamr *et al.* 2020), jojoba oil and astaxanthin (Esumi *et al.* 2021), and pomegranate (Ramio *et al.* 2015; Puigdemont *et al.* 2021).

Formulations

A variety of formulations are available for delivering active ingredients to the skin of atopic dogs.

Shampoos

Shampoos should be considered when haired skin or extensive areas of an atopic dog are affected (Mueller *et al.* 2012). Washing with an appropriate shampoo can reduce or even remove the amount of allergen in the coat, improve the functioning of the skin barrier, and help resolve microbial overgrowth. The shampoo should be left in contact with the skin for about 10 minutes to enable active ingredients to be effective and to allow hydration of the stratum corneum (Miller *et al.* 2013d). Thorough rinsing then leaves the coat soft, shiny and easy to comb. Any cleansing shampoo which enables the mechanical removal of allergens, skin debris and micro-organisms from inflamed skin and coat should temporarily alleviate pruritus, especially if applied with cool water (Curtis 1998) (Figure 5).

Shampoos should lather well, be easily rinsed, leave no residue and be non-irritant to skin and eyes. Although some shampoos contain soaps, which are harder to rinse and in hard water areas can leave a dull film on the coat, many are now surfactant or detergent-based with a wide range of added ingredients such as suspending agents, foam boosters, thickeners, antioxidants, conditioners, colouring agents

and fragrances. As with any medication, a shampoo must be thoughtfully selected and carefully applied in order to achieve optimal benefit and avoid potential problems (Table 4). Excessive washing may result in increased scaling and damage to the skin barrier (Miller *et al.* 2013e; Shimada and Iwasaki 2020).

Two to three per cent chlorhexidine shampoos have been found to be effective against staphylococcal bacteria, and shampoos containing a combination of 2% chlorhexidine and 2% miconazole are effective in dogs with *Malassezia* overgrowth (Mueller *et al.* 2012) (Figure 6). Combination therapy with a 4% chlorhexidine digluconate shampoo, applied twice weekly, and a 4% chlorhexidine digluconate solution, applied once daily on the days when the shampoo was not used, was found to be as effective as systemic clavulanate-potentiated amoxycillin tablets (25 mg/kg every 12 hours) over a 4-week period, in a randomised, blinded study of 51 dogs with superficial pyoderma, conducted in Italy (Borio *et al.* 2015).

Shampoos containing 2–3% benzoyl peroxide are degreasing, antipruritic, and may also be effective against cutaneous bacteria (Mueller *et al.* 2012) (Figure 7).

A shampoo containing lipids, complex sugars and antiseptics (Allermyl, Virbac Limited), and another containing phytosphingosine, raspberry oil and lipids (Douxo Calm, Ceva Animal Health Limited) have been shown to provide a modest effect on skin lesions and pruritus in a small trial of allergic dogs (Bourdeau *et al.* 2007; Bensignor *et al.* 2013).

Although active ingredients are included to enhance the antipruritic properties of shampoos, studies showing that whirlpool baths, with and without a shampoo, can be anti-pruritic (Löflath 2007) suggest that the intensity and frequency of bathing may be the most important factors in relieving pruritus (Olivry *et al.* 2015). A novel microbubble wash system has been reported to clean the skin surface and hair coat of dogs. No scrubbing was needed and impairment of skin barrier function was less than that seen with a control shampoo which contained no moisturising components (Shimada and Iwasaki 2020).

Other formulations

Rinses, powders, lotions, sprays, creams, ointments, foams, mousses, gels and emulsions, wipes, pads, and spot-ons are also available for topical delivery of active ingredients. Choice of formulation depends on a number of factors including the surface area to be treated, presence of hair in the affected area, type of lesion present, and the need for residual activity. Shampoos, rinses, sprays, foams, mousses and spot-ons are practical and effective ways to deliver active ingredients to large areas of skin. Gels, creams, wipes, pads and ointments are good options for less hairy regions, or for localised lesions, for example on the feet or in facial folds (Figures 8-10).

Spot-on products are available for improving epidermal barrier function in atopic dogs. One product (Allerderm Spot-on, Virbac Limited) contains a mixture

of ceramides, fatty acids and cholesterol. Another spot-on product, Pyospot (Dermoscent Laboratories), contains a combination of plant extracts aimed at restoring skin flora balance; ingredients include two herbs ajowan and neem, vegetable oils, tamanu and hemp, essential fatty acids, and essential oils lavender, lemon eucalyptus, palmarosa and savory.

Topical glucocorticoids can in many cases be very helpful in relieving pruritus, especially in dogs with localised pruritus. These products should not be used as sole therapy but as part of an overall management strategy. A spray containing hydrocortisone aceponate (Cortavance, Virbac Limited) is licensed in the UK for symptomatic treatment of inflammatory and pruritic skin disorders in dogs. A gel containing fusidic acid and betamethasone (Isaderm, Dechra Veterinary Products) is licensed in the UK for the treatment of surface pyoderma.

Summary

Topical medications consist of active ingredients in a vehicle that facilitates application to the skin. They have widespread applications in small animal practice, especially in the management of canine atopic dermatitis. Appropriate topical therapy can reduce or, in some cases, eliminate the need for systemic therapy.

References

For a full list of references please visit: www.vetcpd.co.uk/references

Table 4: Some potential benefits and problems with shampooing dogs

Benefits	Problems
• Active ingredients delivered directly to the skin • Reduced need for systemic therapy • Treatment of non-target microbiomes is typically avoided • Minimal risk of side-effects • Removal of micro-organisms and allergens • Soothing • Cleansing • Increased pet-owner bonding • Many dogs enjoy being washed • Typically inexpensive	• Time-consuming • Labour intensive • Poor compliance when frequent application needed • Hard in aggressive or unruly dogs • Some dogs do not like being washed • Clipping sometimes necessary • May trigger irritation or contact dermatitis • Percutaneous absorption or oral ingestion of ingredients • Skin barrier function may be impaired by frequent washing • Possible adverse reaction by owners



Figure 7: Degreasing shampoos are indicated in some atopic dogs.



Figure 8: Acute moist dermatitis can respond well to clipping and topical antimicrobial therapy.



Figure 9: In the interdigital region, wipes are sometimes easier to apply than shampoos.

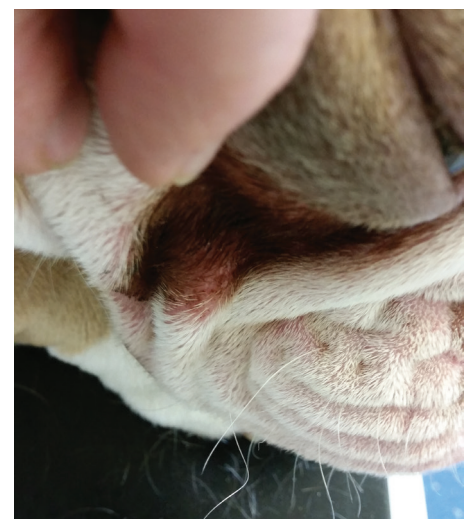


Figure 10: Erythema in facial folds often responds well to antimicrobial wipes.

CLINICAL CASE: Topical therapy in a pruritic Olde English Bulldogge with canine atopic dermatitis

Age, Breed, Sex

One year, Olde English Bulldogge,
Entire male.

History

Referred with a 9-month history of
intermittent, recurrent pruritus and
papular dermatitis.

Initial sign: ventral abdominal collarettes.

Vomiting, breathing difficulties, and
increasing lethargy were reported.

Therapy prior to referral

Cephalexin for most of the five months
prior to presentation at Re-Fur-All
Referrals. No improvement had been seen
following two injections of lokivetmab
(Cytopoint, Zoetis UK Limited) or oral
oclacitinib (Apoquel, Zoetis UK Limited)
(standard doses). Initially had responded
well to oral prednisolone (0.33 mg/kg
SID or every other day) and cephalexin
(15 mg/kg BID, Rilexine, Virbac
Limited) given in combination. Other
therapies included chlorhexidine and
miconazole shampoo (Malaseb, Dechra
Veterinary Products) at varying intervals,
imidacloprid and moxidectin spot-on
(Advocate, Elanco UK AH Limited),
and chlorpheniramine injection (Piriton,
GSK). Shampooing once every 3 weeks
was reported to help control dorsal scaling
for 2–3 days.

Clinical signs on presentation

Pruritus reported. Signs included truncal
scaling and alopecia, facial, interdigital and
ventral pedal erythema, and pedal nodular
lesions. (Figures 1–5).

Laboratory procedures

Skin scrapings and coat brushings: no
evidence of ectoparasites.

Fungal culture: no dermatophytes isolated.

Cytology: 1–2 *Malassezia* on tape strips
from the ventral paw and interdigital
region; some cocci and degenerating
neutrophils in the interdigital region;
NAD on tape strips from the dorsum.

Allergy serology: positive titres to
Dermatophagoides farinae (house dust mites),
Tyrophagus putrescentiae (forage mites),
Kentucky bluegrass, *Alternaria* and
Aspergillus (moulds).

Interim therapy

Cephalexin and oclacitinib (Apoquel,
Zoetis UK Limited) stopped.



Figure 1: Initial presentation.



Figure 2: Dorsal scaling and alopecia.



Figure 3: Flank collarettes, scaling and alopecia.



Figure 4: Interdigital erythema and nodular lesions.



Figure 5: Ventral pedal erythema.



Figure 6: Erythema and crusting on and around the chin.



Figure 7: Improved truncal coat condition, five months after initial presentation.

Capsules containing refined omega-3
fish oil, biotin and natural Vitamin E
(Nutramega, Nutravet): 3 capsules daily.

A shampoo containing 2% chlorhexidine
digluconate and 2% miconazole nitrate
(Malaseb, Dechra Veterinary Products):
frequency increased to twice weekly.
Instructions were given regarding leaving
the shampoo on for ten minutes prior to
rinsing.

Antimicrobial wet wipes containing
chlorhexidine, TrisEDTA, climbazole, and
zinc gluconate (CLX wipes, Nextmune):
1–2 times daily on paws.

A gel containing betamethasone and
fusidic acid, Isaderm (Dechra Veterinary
Products): as necessary in pruritic areas

A spot-on solution containing
imidacloprid and moxidectin: Advocate
Spot-on Solution (Elanco UK AH
Limited): monthly.

Re-examinations After one month

Some increase in pruritus and erythema
following cessation of oclacitinib and
cephalexin. (Figure 6). Therapy was
continued as outlined for interim therapy.

After two months

Sublingual allergen-specific
immunotherapy was introduced.
No systemic antibiotics or systemic
antipruritic treatments were given.
Vomiting, breathing difficulties, and
lethargy resolved. Winston was reported

to be happier in himself, less pruritic and presented with fewer lesions, although pedal pruritus and abdominal papules sometimes recurred.

After one year

Winston was then re-examined at 3-monthly intervals. After one year, he was reported to have been consistently well in himself, and his truncal skin and coat quality were good. Pruritus and transient pedal lesions were reported occasionally. Cytology revealed varying levels of yeast, neutrophils and cocci. Therapy was continued as outlined for interim therapy. Isaderm was used to help control flares. No systemic antibiotics or systemic antipruritic treatments had been given for a year. (Figure 7).

Eventual outcome

Winston remained generally lively, happy and healthy, although some breathing difficulties recurred the following year. Truncal skin remained in good condition. Intermittent pedal pruritus and nodules, mostly controlled by topical therapy. Allergen-specific immunotherapy and omega-3 fatty acid supplementation were maintained.

Diagnosis

Canine atopic dermatitis.

Discussion

The history and clinical signs were consistent with a diagnosis of recurrent atopic dermatitis involving staphylococcal and yeast overgrowths. Skin scrapings, coat brushings, dermatophyte culture, and cytology were performed to investigate the presence of differentials (e.g. ectoparasitic infestations and dermatophytosis) and conditions that could be exacerbating the atopic dermatitis (e.g. bacterial overgrowth and *Malassezia dermatitis*). Atopic dermatitis is a clinical diagnosis. Allergy serology was conducted to identify allergens for allergen-specific immunotherapy (ASIT). Intradermal testing is seen as the gold standard approach for identifying allergens for ASIT, but cost was an issue, and the owners were keen to avoid sedation (necessary for intradermal testing) if possible.

Although the response to systemic glucocorticoid and antibiotic therapy prior to referral appeared to have been good, Winston's owners were keen for him to avoid these drugs if possible. Resolution of adverse systemic reactions (vomiting, lethargy, breathing difficulties) cannot definitively be attributed to

avoidance of systemic glucocorticoids and antibiotics, but vomiting is recognised as a possible adverse reaction in animals treated with cephalexin (Compendium of data sheets, 2021) and glucocorticoids (Elkholly *et al.* 2020). Many adverse reactions can be associated with glucocorticoids including respiratory and behavioural problems (Miller *et al.* 2013 ¹).

A favourable response to washing with an antimicrobial shampoo had previously also been reported, but Winston was then being washed only every three weeks. As improvement was reported to be lasting for only two or three days, it was important to increase the washing frequency to twice weekly. Care was taken not to overwash as frequent washing may cause further dryness and irritation (Miller *et al.* 2013 ²; Olivry *et al.* 2015). A contact time of 10 minutes was advised in line with current recommendations (Frank and Loeffler 2012). The shampoo and wipes, both containing chlorhexidine, were chosen due to the reported antimicrobial efficacy and safety of these products (Mueller *et al.* 2012; Cavana *et al.* 2015).

Twice weekly washing with an antimicrobial shampoo, and daily focal application of antimicrobial wipes, combined with omega-3 fatty acid supplementation and daily sublingual ASIT were generally successful in managing Winston's atopic dermatitis.

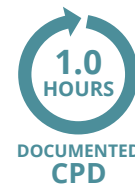
Episodes of pruritus and recurrence of pedal lesions were still reported, but increasing the frequency of Isaderm, as necessary, helped to bring these under control. A cutaneous spray containing hydrocortisone aceponate is licensed in the UK for symptomatic treatment of inflammatory and pruritic dermatoses in dogs. This spray might have also been helpful, but was largely unavailable during the treatment period under discussion.

Topical therapy here was combined with other treatment modalities, and it is hard to be sure of the precise role each played in the favourable overall clinical response. However, treatment of CAD is often multimodal, and it is likely that topical therapy was helpful in improving the patient's skin and coat condition and instrumental in enabling the sustained avoidance of systemic antibiotics and antipruritic agents, and the improved well-being and demeanour of the patient.

References

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