

**Treatment of Canine Atopic Dermatitis**

**Introduction**

Canine Atopic Dermatitis (CAD) is an inflammatory allergic skin disorder, affecting genetically predisposed dogs, with characteristic clinical features\(^7\). CAD affects 3 to 15% of the canine population. In some studies up to 50% of dermatology cases are atopic cases\(^3\). It is generally associated with IgE antibodies most commonly directed against environmental allergies (Type 1 hypersensitivity). The patient becomes sensitised to environmental antigens that cause no reaction in non-atopic dogs. It has also been shown that there are innate as well as acquired defects of the epidermal barrier in atopic dogs. Inherited innate barrier function defects are a significant primary risk factor for CAD. Epidermal barrier defects facilitate contact of allergens with epidermal immune cells. The defective epidermal barrier in addition results in increased transepidermal water loss (TEWL) resulting in dry skin with loss of skin flexibility, increased penetration of irritants and allergens and a lower ability to prevent microbial colonisation\(^5\).

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Figures 1 and 2: Pruritus is the most common clinical sign of CAD

**Treatment principles**

- It is very important to remember that CAD cannot be cured. It can only be managed as well as possible, with the aim to give the patient a better quality of life, as in most cases the dog cannot be protected against allergen exposure\(^3\).
- It is important to remember that every allergic dog has an allergic threshold. The allergic load can often be tolerated by an allergic dog without disease manifestations. A small increase in the load may push the patient over the threshold and cause or initiate clinical signs\(^1\).
- The allergic threshold is not fixed and can be raised or lowered by various trigger factors, such as food, infections (staphylococci and/or Malassezia), external parasites and environmental allergens.
• The threshold may therefore be controlled by treatment of the secondary infections, control of ectoparasites and treatment of any associated adverse food reactions.
• Barrier repair is becoming increasingly important in the management of CAD in dogs. This can be facilitated by bathing regularly with appropriate shampoos and dietary and topical fatty acid supplementation.
• Successful long-term management also requires substantial and ongoing owner commitment. The owners need to understand the concept of the allergic threshold so that they can help to determine and avoid triggering factors and adjust long term management accordingly.

1. Avoidance of allergen:
• In theory this would be the best possible treatment, but usually this is not practical or possible.
• Generally the aim is to decrease exposure. In a case where a dog is allergic to house dust mites, it may help to use a combination of measures. These may include keeping the dog outdoors, away from bedrooms, off fabric furniture, to avoid stuffed toys, using impermeable pet mattress covers and frequent and thorough pet mattress and environment washing and vacuuming. Acaricides that eliminate house dust mites may help, but their benefits are not immediate because the allergens often remain in the environment for a long time.

Figure 7: Every allergic dog has an allergic threshold. The allergic threshold is not fixed and can be raised or lowered by various trigger factors, such as diet, infections (staphylococci and/or Malassezia), external parasites and environmental allergens (Courtesy Royal Canine: Treatment principles for CAD).
One uncontrolled study reported the benefit of house dust mite control with the acaricide benzyl benzoate spray for reduction of clinical signs in house dust mite hypersensitive atopic dogs.

Figures 3 and 4: Erythema and papules on the limbs and feet are typical findings in a CAD case (Photos courtesy of Dr H Schroeder)

Figure 8: Pustules and bacterial collarettes are typical clinical signs of a secondary bacterial pyoderma (Photo courtesy of Dr H Schroeder)

2. Control of secondary infections:

Secondary bacterial infections often complicate CAD. Initial treatment with appropriate systemic antibiotics (e.g. cephalosporins, amoxicillin-clavulanic acid) for a minimum of 3 weeks is usually effective in controlling the secondary bacterial infections. It is often necessary to continue with some form of pulse or weekend treatment to prevent the infections from recurring. Weekend treatment has been shown to be effective in controlling relapses.
Secondary Malassezia infections often exist concurrently with the bacterial infections. Initial treatment with systemic ketoconazole for a minimum of 3 weeks is usually followed by some form of pulse therapy to prevent these infections from relapsing.

The use of topical antimicrobial shampoos may in some cases be sufficient to control the secondary infections without necessitating systemic medications.

Figure 9: Cytology of a bacterial infection with neutrophils and cocci bacteria

Figure 10: Malassezia yeast infections commonly complicate CAD cases
3. Allergen-Specific Immunotherapy (ASIT):

- The cornerstone of CAD treatment is Allergen-Specific Immunotherapy (hypo- sensitisation or desensitisation). This is the practice of administering gradually increasing quantities of an allergen extract to an allergic patient to ameliorate the symptoms associated with subsequent exposure to the causative allergen.

- Immunotherapy should be considered for young patients; patients where concurrent treatment with topical shampoos, systemic antibacterial and anti-yeast medications is not able to control pruritus sufficiently; cases where corticosteroids have to be used at high dosages for control of pruritus or where side effects are unacceptable.

- Response to immunotherapy may take 3 to 10 months.

- Corticosteroids and cyclosporine have multiple effects on the immune reaction. It is recommended to rather avoid their use during immunotherapy, especially during the initial phases. Antihistamines, essential fatty acids and topical therapy are allowed.

- The success rate is 65 – 75%.

- Most cases require lifelong control with immunotherapy, supplemented from time to time with other therapy.

4. Suppression of inflammation:

4.1 Antihistamines:

- H1 antihistamines may sometimes give partial relief to the pruritic patient.

- They are usually used in conjunction with prednisolone to help lower the dose of prednisolone required to control the pruritus and inflammation.

- A selected antihistamine should be administered for 10 to 15 days before evaluating its effectiveness.

- Antihistamines commonly used, together with dosages, are given in the table below.
### ANTIHISTAMINES

<table>
<thead>
<tr>
<th>Antihistamine</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Chlorpheniramine</td>
<td>0.4 mg/kg q8h</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>2.2 mg/kg q8h</td>
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<tr>
<td>Hydroxyzine</td>
<td>2.2 mg/kg q8h</td>
</tr>
<tr>
<td>Loratidine</td>
<td>0.25-1 mg/kg q24h</td>
</tr>
<tr>
<td>Clemastine</td>
<td>0.1-0.25 mg/kg q12h</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>2.5-20 mg q24h</td>
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### 4.2 Corticosteroids:

- These drugs are highly effective in relieving pruritus, except when fleas or other ectoparasites and/or severe bacterial and/or Malassezia infections are present concurrently.

- Corticosteroids have various anti-inflammatory properties. They are strong inhibitors of the synthesis of pro-inflammatory cytokines with keratinocytes and Langerhans cells their principal targets.

- They are used in many CAD cases and have been one of the most commonly prescribed drugs over the past years for the treatment of CAD.

- Once the secondary infections and other complications have been treated and the patient is still pruritic, it is one of the treatment options for patients where immunotherapy is not a treatment option.

- In cases where corticosteroids have to be used, the following rules should be followed:
  1. Use only short acting, oral products, e.g. prednisolone, prednisone and methyl prednisolone. Prednisolone and prednisone are equally effective in dogs.
  2. Ideally use an alternate-day regime often together with antihistamines and essential fatty acids, which makes it possible to reduce the dose of corticosteroid required.
  3. Start with 1 mg/kg once a day and halve the dose every 4 to 5 days. A maintenance dose of ½ mg/kg every other day or less is considered “safe”.
4. The use of injectable forms, especially the “long acting” corticosteroids, is not advised due to the high risk of side effects.

5. A patient on chronic corticosteroid therapy should be examined every three months to monitor weight, inspect the skin for infectious complications and check the urine for urinary tract infections which are very common in these patients.

4.3 Oral Essential fatty acids (EFAs):

- EFAs have a significant anti-inflammatory action and assist to restore the barrier function of the skin if used in formulations with sufficient quantities of omega-3 and omega-6 EFAs in a ratio close to 5:1\(^8\).

- EFA therapy appears to be dose-responsive. The studies that reported a good response to EFA therapy were studies in which the highest doses of EFAs were given\(^10\). Recommended effective dosages are omega-6 at 150 mg/kg and omega-3 at 30 mg/kg\(^8\).

- In their practical guidelines paper\(^17\), the Canine Atopic Dermatitis Task Force conclude that EFAs have a role to play in the management of chronic CAD, but there is still no consensus regarding particular combination, dosage, ratio and formulation (including enriched diets)\(^17\).

- EFAs require up to 2 months of supplementation before any benefit might be seen\(^8\).

- They are not suitable for monotherapy of CAD, but rather as part of the management programme\(^18\).

- EFAs are considered corticosteroid reducing agents, because when used in combination with antihistamines, antimicrobial agents, topical medications and medicated shampoos, they have been shown to reduce the dosage corticosteroid required\(^18\).

- Many commercially available dog foods have added omega-3 and omega-6 fatty acids. Diets supplemented with “optimum” ratios EFAs have revealed a reduction in pruritus of at least 50% in 43 – 45% of dogs with CAD in two studies\(^20, 21\).

4.4 Cyclosporine:

- Oral cyclosporine is a thoroughly evaluated drug for the treatment of CAD. It is a calcineurin inhibitor.
Cyclosporine acts mainly on T helper lymphocytes. It also acts on mast cells, eosinophils and Langerhans cells, reducing their antigen presentation functions and inhibits the synthesis of keratinocyte associated cytokines and prevents delayed hypersensitivity reactions\textsuperscript{17}.

This drug is used as an alternative to corticosteroids to control pruritus. It reduces pruritus and cutaneous lesions. At a dose of 5 mg/kg/day, it was found to be equally as effective as prednisolone\textsuperscript{4}.

For maximum absorption it should be administered 2 hours before a meal\textsuperscript{12}.

A lag period of about 2-3 weeks in which no response is seen, occurs after cyclosporine treatment is started\textsuperscript{12}.

Significant reduction in pruritus is expected in 75 – 85% of cases within 1 month of treatment\textsuperscript{12}.

After six weeks, alternate day therapy and even twice weekly treatment has been effective.

It is safe in dogs and does not cause nephrotoxicity nor does it induce arterial hypertension as in humans. Vomiting and diarrhoea are the most commonly seen adverse effects in dogs. This is seen in 14 – 42% of cases, but is mostly mild to moderate. Papillomatous eruptions and gingival hyperplasia are occasionally seen\textsuperscript{4}.

The drug is unfortunately very expensive for use in large dogs.

5. **Stress control:**
   - Stress and anxiety can be triggers that can cause a flare up in an allergic patient’s condition\textsuperscript{3}.
   - Examples include boarding, family going on holiday, loss of a family member, a new baby or pet or moving to a new home\textsuperscript{3}.
   - Some of the anti-histamines (e.g. hydroxyzine, cetirizine, clemastine) or serotonin reuptake inhibitors (e.g. fluoxetine, clomipramine) may be helpful in treating CAD because of these anti-anxiety effects\textsuperscript{16}.

6. **Topical treatment:**
   Topical treatment is a very important component in effective management of CAD and includes shampoos, topical lipids, sprays, creams and ointments.
6.1 Shampoos

- Shampoos rehydrate the skin and result in the patient looking, smelling and feeling better.
- They help to remove allergens from the skin surface, help to restore the epidermal barrier and help to control inflammation and secondary skin infections.
- There are a variety of shampoos available that may be helpful in the management of an allergic skin disease:

6.1.1 Cleansing, non-irritating shampoos

These shampoos are used to improve or restore the epidermal barrier, e.g. EFA treatment shampoos, hypoallergenic shampoos, shampoos containing ceramides.

6.1.2 Soothing shampoos

- Colloidal oatmeal is a safe and effective soothing antipruritic agent, commonly used in shampoos. The exact mechanism of this effect is poorly understood. This agent is safe, only provides short term relief (24-48 hours) of mild pruritus and has no antimicrobial properties. EFA treatment shampoos have soothing effects because they are rich in essential fatty acids and essential oils, with a natural soothing agent from pumpkin seeds. These shampoos also rehydrate the skin and reinforce skin barrier function.

6.1.3 Antimicrobial shampoos

Antimicrobial shampoos may be used to control secondary bacterial and/or yeast infections. Antimicrobial agents include:

- **Chlorhexidine digluconate:** An antiseptic effective against most bacteria, fungi and *Malassezia pachydermatis*. It is bactericidal by action on the cytoplasmic membrane, which causes leaking of intracellular components, is characterised by a rapid kill, has a 36-hour residual activity and is non-toxic and non-irritant. In a study by Jasmin *et al* a 3% chlorhexidine shampoo was highly effective in the treatment of Malassezia dermatitis and concurrent bacterial pyoderma when present.
- **Povidone-iodine**: An iodophore which slowly releases iodine to tissue. It is an effective broad-spectrum antimicrobial and is useful for local lesions. It has a prophylactic effect because of its persistence on the skin, but should not be used repeatedly for generalized skin problems due to its irritant and staining properties.

- **Benzoyl peroxide**: It is metabolised in the skin to benzoic acid. Much of its microbicidal activity derives from the lowered skin pH which disrupts microbial cell membranes. It is also an oxidizing agent, which releases nascent oxygen into the skin and produces a series of chemical reactions resulting in permeability changes and rupture of bacterial membranes. It has an excellent prophylactic effect and its follicular flushing, keratolytic degreasing and comedolytic activity are additional benefits. It is generally used in concentrations of 2 to 3%, which are well tolerated, but irritation can occur at higher concentrations (erythema, pruritus and pain).

- **Quaternary ammonium compounds**: They are surface acting agents. They have less effect and are only useful for limited bacterial involvement. They have no residual effect and have to be applied often for good effect.

### 6.1.4 Keratomodulating shampoos

These shampoos are indicated in cases with allergy induced keratoseborrhoeic changes. Keratomodulating agents include:

- **Salicylic acid** (0, 5 – 2%) is keratolytic. It causes a reduction in skin pH, which leads to increased hydration of keratin. These actions help to soften the corneal layer. It acts synergistically with sulphur and is often present in small quantities in shampoos.

- **Sulphur** (0, 5% - 2 %) is mildly keratolytic (forms hydrogen sulphide in the stratum corneum), keratoplastic (has a direct cytostatic effect) and has numerous antiseborrheic effects.

### 6.1.5 Combination shampoo

A shampoo specifically designed for CAD has recently been developed. It restores and maintains the epidermal barrier function, controls aggravating microbial proliferation, and limits immune and inflammatory reactions. The ingredients are linoleic acid (LA) and gamma-linolenic acid (GLA), EFAs that restore the skin barrier; piroctone olamine, an antiseptic agent effective against bacteria and yeasts; specific monosaccharides, immunomodulator agents and Vitamin E, an antioxidant which has anti-inflammatory and immunostimulatory effects.

### 6.2 Topical lipids
- Topical lipids have been used with success in improving the epidermal barrier in human atopic dermatitis\(^\text{15}\).

- There are a few published studies in the veterinary literature that have documented the effects of topical fatty acids on the barrier function in dogs.

- In a study by Muller and Tretter\(^\text{24}\) the topical application of either a fatty acid containing spot-on (Dermoscent® Essential 6® spot-on, LDCA, France) (applied weekly) or spray (Atop 7® spray, LCDA, France) (applied daily) improved both the lesions and pruritus in dogs with CAD\(^\text{24}\).

- A study by Blaskovic and colleagues\(^\text{2}\) evaluated the effects of a spot-on formulation containing essential fatty acids on the clinical signs of CAD. Their study showed that the spot-on formulation (Dermoscent® Essential 6® spot-on, LDCA, France) applied weekly for 8 weeks was beneficial in alleviating the clinical signs of both mild and severe cases of CAD\(^\text{2}\).

- A study by Piekutowska and Pin\(^\text{19}\) demonstrated an increase in epidermal lamellar lipids. This suggested that treatment with topical lipids (Allerderm® spot-on, Virbac SA, France) stimulated the production and secretion of endogenous \textit{stratum corneum} lipids, contributing to the formation of an improved epidermal barrier\(^\text{19}\).

- Topical lipid products available in South Africa, both are spot on formulations.

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<thead>
<tr>
<th>Product</th>
<th>Ingredients</th>
<th>Formulations</th>
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<tbody>
<tr>
<td>Dermoscent® Essential 6® spot-on</td>
<td>EFAs, Essential oils, Vit E</td>
<td>Spot on</td>
</tr>
<tr>
<td>Allerderm® spot-on</td>
<td>EFAs, Ceramides</td>
<td>Spot on</td>
</tr>
</tbody>
</table>

- Topical lipids are more effective in restoring the hydrolipidic film faster when compared to oral EFAs\(^\text{9}\).

- Dermoscent® Essential 6® spot-on also moderates sebaceous gland activity and sebum production, rebalances dry or oily coat and skin, is skin barrier enhancing and reduces TEWL for optimal skin hydration\(^\text{9}\).

\textbf{6.3 Topical spray:}

- A steroid-free topical spray (Atop 7® spray, LCDA, France) has been developed for the symptomatic treatment of CAD. It has 100% natural active ingredients which have a synergetic efficacy and does not have any side effect of steroids.
ATOP 7. The spray is soothing, reduces skin inflammation, regenerates and repairs the epidermal barrier, decreases TEWL and has antimicrobial properties.

### 6.4 Other topical treatments:

- **Topical glucocorticoids**: are useful in Veterinary Dermatology. They are the sole ingredient or part of combination formulations with antimicrobial and other agents and are useful for localized lesions. Tachyphylaxis, atrophy and microbial infections can occur in cases of overuse.

- **Immunomodulators**: Tacrolimus, a calcineurin inhibitor has been shown to be effective in the treatment of localized lesions of CAD.

- **Antibiotics**: formulations containing fusidic acid and mupirocin are useful for treating localized lesions of pyoderma.

- **Antifungals**: products containing azole derivatives or nystatin can be used on localized lesions of dermatophytosis, Malassezia dermatitis or candidiasis.

### Conclusions

- Effective management of a CAD case requires combination therapy.

  The basis of the therapeutic approach is ASIT, together with concurrent medical therapy including antimicrobials, EFAs and the frequent use of topical shampoo and topical lipids.

- With good management the use of corticosteroids will be considerably reduced.

- Successful management depends on a thorough understanding of the pathogenesis and of the potential trigger factors and complications, and on a willingness to modify the therapy in the light of a changing situation.

### References


9. Dermoscent training KSD and atopy, Afrivet, Pretoria


cutaneous Malassezia populations and associated clinical signs (Malassezia dermatitis) in dogs. *Proceedings of the Annual congress of the ESVD-ECVD, Tenerife, Spain, 4-6 September 2003:* 170


