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## CANINE ATOPIC DERMATITIS: EVIDENCE BASED DERMATOLOGY

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### DEFINITION

The American College of Veterinary Dermatology defines canine atopic dermatitis (CAD) as a genetically- predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features which most commonly is associated with IgE antibodies to environmental antibodies.

### INCIDENCE AND PREVALENCE

Neither the incidence nor the prevalence of atopic dermatitis in the general canine population has been studied. Most textbooks estimate a prevalence of around 10%. In a recent study of over 31,000 dogs examined by veterinarians in 52 private veterinary clinics in the USA, 8.7% of the dogs were diagnosed with atopic dermatitis. In human beings there is an increasing incidence of atopic diseases, which is suspected to be caused by environmental rather than genetic factors. Something similar is probably also happening in the case of canine atopic dermatitis.

### PATHOGENESIS

Most dogs with AD develop an IgE mediated hypersensitivity reaction against environmental allergens that enter percutaneously in the organism. Other factors as secondary bacterial infections also help to maintain a chronic inflammatory reaction in the skin.

### CLINICAL MANIFESTATIONS

#### Age of onset

Between 6 months and 3 years.

#### Breed Predispositions

Breed predispositions are definitively seen in atopic dermatitis, but national or regional variations probably exist, and predispositions could change over time. Most studies report the following breeds to be at higher risk: Beauceron, boxer, Chinese shar pei, cocker spaniel, dalmatian, English bulldog, setter, Boston terrier, Cairn terrier, Scottish terrier, West Highland white terrier, Yorkshire terrier.

#### Sex predilections

Reports of sex predilections are inconsistent, thus for the present, this issue should be considered unresolved.

#### Seasonality

CAD can be seasonal or nonseasonal, depending on the allergens involved. The majority of dogs with AD will exhibit nonseasonal clinical signs.

#### Anatomical Location of Pruritus

A typical dog with AD will exhibit pruritus of the face, ears, paws, extremities and/or ventrum. Any one, any combination or all these areas can be affected.

#### Primary Lesions

The consensus appears to be that some dogs with AD have no visible primary lesions, even in the pruritic areas, and that the primary lesions of AD (when present) would

consist primarily of erythema. Secondary lesions, consequence of chronicity and scratching or of secondary infections are common, and include: red-brown salivary staining, excoriations, self-induced alopecia, papules, collarettes, crusts, hyperpigmentation and lichenification.

### Additional Features of AD

Otitis externa is very common, occurring at least historically in as many as 86% of dogs. Conjunctivitis is present in as many as 50% of patients. Acute moist dermatitis, acral pruritic nodules and bacterial pododermatitis are other potential secondary manifestations of AD. Marked seborrhea is described in 12-23% of patients.

### DIAGNOSIS OF CAD

There is good consensus that the diagnosis of CAD is made clinically according to:

1. Compatible clinical picture
2. Elimination of other diseases than can cause the clinical picture (flea allergy dermatitis, scabies, food hypersensitivity, *Malassezia* dermatitis, bacterial folliculitis)

A system based in the fulfillment of a few selected criteria, as done in human dermatology, has been proposed. Unfortunately, these criteria never were evaluated. More recently, a list of five major criteria for CAD was proposed by Prélard et al (1998) using a survey seven veterinarians examining 96 canine patients. The presence of three out of five of these criteria in a patient resulted in sensibility and specificity of approximately 80%.

#### Clinical Criteria for Diagnosis (Prélard et al 1998)

Corticosteroid-sensitive pruritus

Erythema of the pinnae

Bilateral cranial erythematous pododermatitis

Cheilitis

Appearance of first signs between the ages of 6 months and 3 years

Following initial clinical diagnosis of AD, one of the several diagnostic tests is often performed, to confirm the diagnosis and to identify the allergens involved. The tests (both in vivo and in vitro) should not be used as screening tests for allergy in a pruritic animal. They should only be considered if there is strong clinical evidence for allergy, and after all other possible diagnoses have been eliminated from consideration. The true utility of "allergy tests" could be in the substantiation of a careful clinical diagnosis, but mostly in selection of candidate allergens for immunotherapy.

#### **Laboratory Evaluation of Dogs with AD with Serum-based Tests**

Serum-based in vitro "allergy-tests" are commercially available to veterinarians, and are widely used. Following initial clinical diagnosis, panels of allergen-specific IgE measurements may be performed in an attempt to identify to which allergens the atopic dog is hypersensitive. Methodology for these tests varies by laboratory, few clinical studies have evaluated performance of these tests, and current inter-laboratory standardization and quality control measures are inadequate. In any case, remember that these

tests are IGE-tests, not allergy tests. The usefulness of these tests can be greatly improved through appropriate use.

### Evaluation of Dogs with AD with Intradermal Testing (IDT)

In the dog are performed using aqueous allergen extracts. Although optimal concentrations of allergens for use in IDT in dogs have been not rigorously studied, in the absence of more scientific evidence the ACVD recommends following dilutions:

Pollens, molds:	1000 PNU/ml
Individual house dust mites:	50 000 W/v
Cattle hair, wool, feathers, silk	250-500 PNU/ml
Insects	1000 PNU/ml

There is consensus that only extracts containing individual allergens should be used for IDT in dogs. The patient preparation is also very important. Many drugs adversely affect reactivity of the skin to allergens in the IST: antihistamines (hydroxyzine), tricyclic antidepressants (doxepin), and glucocorticoids. IDT can be performed on non-sedated dogs; however, most dermatologists prefer to use sedation as the improved patient compliance allows for a more easily performed and convenient testing. Sedatives and anesthetics that do not affect skin reactivity and are acceptable for IDT include: xylazine hydrochloride, medetomidine, tiletamine, thiamylal, halothane, isoflurane and methoxyflurane. Oxymorphone, ketamine/diazepam, acepromazine and propofol can adversely affect the IDT and should not be used. Most dermatologists perform the IDT on the lateral thorax. The site is gently shaved but should not be scrubbed or washed.

Typically, a volume of 0.05 ml of solution is injected intradermally. Reactions are evaluated 15 minutes after injection. By convention, reactions are usually recorded with a score designated as 0, 1, 2, 3, or 4; where 0 is equal to the reaction of the negative control and 4 is equal to the reaction of the positive control. Any reaction of 2 or greater is regarded as positive.

### HISTOPATHOLOGY OF CAD

Recent studies have established that canine atopic skin lesions exhibit an inflammatory pattern characterized as a chronic, hyperplastic and spongiotic, mixed perivascular dermatitis. The nature of epidermal and dermal inflammatory infiltrate has now been characterized using immunological techniques. Epitheliotropic cells include Langerhan's cells, T-lymphocytes and eosinophils. Dermal cells are composed of mast cells, dermal antigen-presenting cells, T-lymphocytes and occasional intact and degranulated eosinophils.

### THERAPY

The treatment of AD is multifaceted and consists of a combination of anti-inflammatory agents, allergen-specific immunotherapy and antimicrobial drugs. Each patient should be approached in a different way, considering factors as severity, seasonality and presence of secondary infections. General principles of therapy are:

- i) An effective flea control programme should be followed in all patients.
- ii) Frequent bathing of patients, specially using specifically designed shampoos are helpful in reducing pruritus in most patients.

- iii) Control of secondary bacterial and yeast (*Malassezia*) infections is also mandatory.

### Pharmacotherapy

**Glucocorticoids (G's).** There is good evidence about efficacy of oral GCs in the treatment of CAD. Prednisone 0.75-1 mg/Kg/day for 7 days and then each 48h is effective in over 75% of patients. The ACVD do not recommend the use of long-lasting GC formulations for the treatment of CAD. Side effects of oral GC therapy range from annoying (polyuria, polydipsia, polyphagia, obesity, alopecia) to potentially life-threatening clinical signs (pancreatitis, gastrointestinal ulceration...). Long-term administration of oral GC for the treatment of allergic skin diseases almost inevitably triggers the appearance of bacterial urinary tract infections.

**Antihistamines.** There is not good evidence at present time regarding efficacy of antihistamines in the therapy of CAD. A critical review of literature describing antihistamines therapy in CAD reveals that the majority of published studies are open uncontrolled or only partially controlled trials. The studies published consider that hydroxyzine, clemastine and chlorpheniramine are probably the most effective. Considering scientific evidence and clinical experience, the ACVD concludes that: (1) Beneficial effects are seen only in a few dogs, (2) Response to treatment varies widely by patient and by drug, therefore is necessary in each patient to conduct a serial trial of a variety of antihistamines, (3) The beneficial effect occurs within the 7-14 days of treatment, (4) antihistamines may be synergistic with GCs, (5) Sedative actions may in part be responsible for clinical benefit.

**Nonsteroidal anti-inflammatory drugs.** There is at present time good evidence that cyclosporine A (CsA, 5mg/kg/day, then EOD, then twice a week) is effective and safe in the control of CAD. The effects of cyclosporine therapy appear only after 4 weeks of therapy. Different studies suggest that the efficacy of CsA is similar to that of GCs, but side effects are much lower and more benign and the patients remain in remission for a longer period of time after CsA therapy than after GCs. Topical tacrolimus has also demonstrated be effective. Different studies have demonstrated some efficacy of drugs as misoprostol, leukotriene inhibitors, phospho diesterase inhibitors (arophylline and pentoxifylline), fluoxetine and capsaicin but the efficacy is too low or the side effects too severe to recommend their use.

**Essential Fatty Acids (EFAs).** Despite theoretical mechanistic reasons for the usefulness of EFA, and results from studies reporting that EFAs could be of benefit for the treatment of CAD, it is still unclear if, when and how EFAs should be recommend as part of the overall management of dogs with this disease.

**Allergen-specific Immunotherapy (ASIT).** In spite of insufficient evidence derived from randomized controlled trials, multiple open studies and a large body of clinical observations suggest that ASIT is effective in controlling the clinical signs of dogs with AD. There are numerous protocols, and a published efficacy of about 50% of cases. However, there is an urgent need for further research to clarify: (1) True efficacy, (2) Historical, clinical and immunologic features that may be predictive of response to ASIT, (3) Protocol of ASIT

with optimal efficacy, (4) Effects of Gcs and other anti-inflammatory drugs on the efficacy, (5) Effects of early detection and early ASIT on the course of the disease.

#### REFERENCE

1. Olivry T (Ed.). The American College of Veterinary Dermatology Task Force on Canine Atopic Dermatitis. *Vet Immunol Immunopathol* 2001; 81:143-387