DEFINITION

Canine atopic dermatitis (CAD) has recently been redefined by the International Taskforce on Canine Atopic Dermatitis as: 'a genetically predisposed inflammatory and pruritic skin disease with characteristic clinical features associated with IgE antibodies most commonly to environmental allergens'. But in around 10% of cases of classical atopic dermatitis no IgE is demonstrable. Such cases are termed 'atopic-like dermatitis', whose definition is: 'a genetically predisposed inflammatory and pruritic skin disease with clinical features identical to those of atopic dermatitis in which IgE antibodies to environmental allergens are not demonstrable'.

CLINICAL SIGNS AND DIAGNOSIS

Breeds over-represented include: Labrador Retriever, Golden Retriever, West Highland White Terrier, Chinese Shar-Pei, Bull Terrier, Bichon Frisé, Tibetan Terrier, English Springer Spaniel, Boxer, French Bulldog, Dalmatian, Vizsla and Basset Hound. Peak onset is 1–2 years of age, with 16% commencing prior to 1 year. It almost never commences below 3 months of age, and rarely before 6 months or after 7 years of age. In Europe most cases are perennially affected, but in North America many are seasonal, with some in time becoming perennial.

Primary Disease

The cardinal sign is pruritus, and initially there may be little evidence of inflammation with erythematous macules and papules developing later. The distribution is predominantly ventral, facial and pedal, which reflects the route of access of allergen and the mast cell density. Most animals suffer from otitis at some point, which in the early stages involves the inner ear flap and vertical canal. The horizontal canal becomes secondarily infected in chronic cases, with accompanying secondary pathological changes. In some cases otitis is the only sign.

Secondary Complications

In time, evidence of self-trauma, hair loss and seborrhoeic changes develop with hyperpigmentation, lichenification and crusting. Bacterial overgrowth, overt pyoderma, Malassezia overgrowth and Malassezia dermatitis are frequent complications.

The Demonstration of Allergen-Specific IGE

The diagnosis of CAD is made clinically, but most dermatologists undertake either intradermal testing (IDT) or serology for allergen-specific IgE, although theoretically this is only necessary to distinguish between CAD and atopic-like dermatitis and to enable selection of allergens for immunotherapy. IDT has been viewed as the 'gold standard', but a recent study questions its reliability, and it is likely that serology is at least as reliable.

Making the Final Diagnosis - Are Diagnostic Criteria Helpful?
A number of studies employing specific diagnostic criteria have been reported, but all have limited sensitivity and specificity. The demonstration of compatible clinical signs and absence of other possible reasons for the presence of these signs remains the preferred approach.

**The Role of Adverse Food Reactions in CAD**

Some 30–50% of cases of CAD that show perennial pruritus are complicated by a coexistent adverse food reaction (AFR). Although the clinical signs of AFRs may be identical to CAD, there are distinguishing features:

- There are different genetic predispositions with the Pug, Rhodesian Ridgeback and German Shepherd Dog specifically predisposed.
- The age of onset differs, with 42% of cases commencing prior to 1 year of age.
- Clinical signs sometimes differ, with otitis sometimes affecting the horizontal canal initially, with perianal involvement in some cases and less prominent volar interdigital involvement.
- There are often concomitant gastrointestinal signs.

However, it is essential that all CAD cases manifesting perennial pruritus be assessed for possible co-existent AFRs prior to embarking on therapy.

**HOW DOES CAD DEVELOP?**

Recent in-depth investigation of clinical cases and of a high-IgE producing strain of Beagles which develop CAD have identified two major defects predisposing to the disease:

- Animals have impaired skin barrier function associated with abnormal filaggrin and lowered amounts of ceramides in their surface lipid. This facilitates allergen penetration.
- They have a Th1/Th2 imbalance favouring the development of IgE. This is associated with interleukin (IL)-4 and IL-13, and lowered production of interferon-γ.

**Route of Access of Allergen**

The condition was previously termed 'allergic inhalant dermatitis', but the main route of allergen access is percutaneous with allergen capture by Langerhans' cells armed with IgE antibody.

**Allergens Implicated**

Pollen allergens of trees, weeds and grasses are commonly implicated, as are human and animal danders. Moulds are involved in a very small percentage of cases. Most important are house dust mites followed by allergens of storage mites. The former have very special roles and induce pro-inflammatory cytokines from keratinocytes, cleave ceramides affecting barrier function and cleave CD23 from activated B cells, thus dysregulating IgE synthesis.

**The Development of Secondary Complications**

- Bacterial overgrowth and staphylococcal pyoderma. Factors predisposing to this include:
  - The carriage rate of *Staphylococcus pseudintermedius* is higher in atopics than in normal dogs.
  - Staphylococci adhere more readily to corneocytes of atopic dogs, and especially to inflamed skin.
IgE-mediated hypersensitivity (and probably also cell-mediated (delayed) hypersensitivity) readily develops.

Some staphylococcal antigens act as superantigens, which have been shown to have significant proinflammatory effects.

- *Malassezia* overgrowth and *Malassezia* dermatitis. The factors predisposing to overgrowth of *Malassezia* are less clear although the propensity for atopic dogs to develop *Malassezia*-specific IgE has been documented.
- Flea allergy dermatitis. Atopic dogs are predisposed to develop flea hypersensitivity.

Thus the atopic dog is:

- A pyoderma waiting to happen
- *Malassezia* dermatitis waiting to happen, and
- Flea allergy dermatitis waiting to happen

**HOW CAN THIS KNOWLEDGE BE USED TO OPTIMISE THERAPY?**

**Key Points**

- There is no 'one-size-fits-all' treatment for CAD.
- The treatment must be optimised for the particular case.
- The treatment is multifaceted.
- The therapeutic plan must embrace the primary defects and the secondary complications.
- The preferred treatment may change over time as the disease changes.

**Managing the Primary Defects**

- The immunological abnormality. Options available include:
  - Allergen-specific immunotherapy (ASIT) - this is the cornerstone of the approach, with success rate of 60–70%, and can be used concomitantly with corticosteroids.
  - Ciclosporin (Atopica®, Novartis) - this has about the same efficacy rate, and again can be given concomitantly with immunotherapy.
  - Corticosteroids. Parenteral products should be limited to short courses, or low-dose alternate-day therapy but are contraindicated where there is a significant secondary pyoderma. Topical products can be used for problem areas and as adjunctive therapy. Hydrocortisone aceponate (Cortevance®, Virbac), which is metabolised in the skin, has received good reports.
  - Antihistamines and essential fatty acids (EFAs) are helpful in a relatively small proportion of cases with 4–6 weeks necessary for EFAs to exert maximum effect.
- Allergen eviction. If there is no allergen, there will not be disease. Examples where this might be done include:
  - House dust mites - these mites live on human and animal dander, and concentration is highest where most time is spent. Products containing permethrin and an insect growth regulator are indicated, with the UV
light stable pyriproxifen being preferable. Note that it takes up to 4 months of continued application before the mite antigens are no longer detectable.

- Storage mites - these live predominantly on poorly stored food, but may be found where there is any vegetable material. Keeping dry food tightly sealed and dry is helpful.

- Managing the barrier defect. This can be done from the outside-in and from the inside-out in the following ways:
  - Shampoos or spot products containing ceramides or their precursors should be maintained for several months until the disease is controlled.
  - Oral EFAs are also capable of restoration of barrier function. It seems logical to use a combination of approaches.

**Managing the Secondary Complications**

- *Malassezia* overgrowth and dermatitis. This can be achieved by:
  - Shampoo therapy with chlorhexidine-based shampoos with or without the addition of azoles. This is the preferred treatment for all but severely affected cases.
  - Oral therapy with itraconazole or ketoconazole, which is best reserved for chronic, difficult cases.

- Bacterial overgrowth and pyoderma. This is one of the most difficult challenges, and is a key to overall success. Key points include:
  - Methicillin-resistant *S. pseudintermedius* is spreading rapidly in Europe and North America, and methicillin-resistant *S. schleiferi* is increasingly important.
  - The most significant factor in resistance development is antibiotic usage.
  - With this in mind, for all but severe cases, shampoo or other topical therapy is the preferred approach.
  - Chlorhexidine-based shampoos are especially useful as they are effective within 1 minute of contact time.
  - The infection will likely recur until the primary defects are eliminated.

**FINAL POINTS**

- Is CAD ever ‘cured’? Certainly some 15–20% of cases may in time require no further therapy. However, one cannot be sure whether this represents spontaneous remission or a result of treatment.

- What do we do about cases of atopic-like dermatitis? There is no specific therapy, and symptomatic therapy alone is used.

- Every case must leave the veterinarian's office with multiple therapies - no one treatment on its own is going to be effective.

**References**

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