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The ACVD task force on canine atopic dermatitis (XV): fundamental concepts in clinical diagnosis

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Abstract

The clinical signs of atopic dermatitis (AD) in man and in dogs are variable, and there is no single physical or historical feature that, if present, indicates the presence of AD. The initial diagnosis of AD is made clinically with the fulfillment of a combination of criteria that are strongly associated with the disease. Several schemes have been proposed in an attempt to define uniform clinical criteria for diagnosing canine AD, but no system is perfect. Once AD is considered as a possible diagnosis, other important differential diagnoses must be methodically eliminated from consideration. As a final step, once the clinician is certain that AD is probable, ''allergy'' tests may be conducted to provide additional evidence to ''substantiate'' the diagnosis. It is important to understand that allergy testing, in whatever form, is not appropriately used early in the patient evaluation as a screening test. Rather, it should be reserved, after a firm clinical diagnosis of AD has been made, to implement allergen avoidance schemes or to select allergens to be incorporated in immunotherapy formulations.

Keywords: Atopy; Allergy; Dermatitis; Diagnosis; Dog; Hypersensitivity

1. Introduction

In human beings and in dogs, atopic dermatitis (AD) has no pathognomonic clinical feature that permits a definitive diagnosis upon initial patient or owner interview and physical examination. Rather, diagnosis is based upon the fulfillment of at least a part of a constellation of strongly associated clinical criteria along with the elimination of other relevant differential diagnoses. Following clinical diagnosis, laboratory or clinical evaluations such as serum-based or intradermal allergy tests, and histopathology of skin biopsy

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specimens merely provide additional evidence to strengthen the case for definitive diagnosis. These evaluations, however, are not foolproof tests for ''diagnosing'' AD.

It must be emphasized that no particular clinical or historical feature, no single test result, and no particular response to therapeutic intervention will *ever* reliably confirm the diagnosis of AD. Indeed, perhaps the only way to unequivocally diagnose a hypersensitivity state would be provocative testing, wherein clinical signs are induced with intentional, controlled allergen exposure. Such manipulations are at best difficult or impractical, and at worst impossible or dangerous for the patient. In case of respiratory allergy in humans, provocative testing via allergen inhalation can demonstrate sensitivity in experimental models (Popa, 1980; Schellenberg et al., 1991). Adverse food reactions are similarly confirmed with exacerbation or recrudescence of clinical signs upon ingestion of allergenic foods using elimination diets and/or double-blind placebo-controlled food trials (Sampson, 1998; Scott et al., 2000). For AD, the atopy patch test (APT) has been proposed as an objective method of diagnosis by inducing typical lesions upon epicutaneous allergen exposure. To date, however, the use of APT has been limited to research studies in humans (Darsow et al., 1995, 1999; Langeveld-Wildschut et al., 1996) and was deemed unreliable in one study with few canine patients with AD (Frank and McEntee, 1995). In contrast to these early results, recent unpublished preliminary data support the feasibility and usefulness of APT in canine species.[1]

Thus, as a consequence of variability in clinical signs and inaccuracies in diagnostic tests, in both human and canine patients, a diagnosis of AD is made using a combination of diagnostic criteria with the ''balance of evidence'' supporting AD and refuting other possible causes of skin disease.

2. Clinical diagnostic criteria for AD

Despite the fact that not one symptom appears consistently in all human AD patients, the principal features include severe pruritus, a chronic-relapsing course, a history of other allergic disease, and a group of typical findings upon dermatological examination (Boguniewicz and Leung, 1998). These typical findings have been arranged by various study groups into lists of clinical diagnostic criteria having a strong association with AD. Physicians then use these criteria as a crude ''checklist'' for initial diagnosis. Examples of these lists are shown in Table 1. It is important to note that certain of these criteria appearing on some lists were shown to have a high degree of variability between physician observers, and thus were considered unreliable (Williams et al., 1994a, b).

A similar list of criteria was extrapolated for canine AD by Willemse in the mid-1980s (Table 1), and many veterinary dermatologists have considered these criteria in evaluation of potentially allergic dogs (Willemse, 1986, 1988). Unfortunately, these criteria never

[1] Olivry, T., Geoly, F., Dunston, S.M., Clarke, K.B., McCall, C.A., 2001. Histological and immunohistochemical characterization of ''atopy patch tests'' in IgE hyperresponsive beagle dogs: a pilot study. Proceedings of the Annual Meeting of American Academy of Veterinary Dermatology and American College of Veterinary Dermatology, Norfolk, VA, p. 38.

Table 1
Clinical criteria for diagnosis of atopic dermatitis in human beings and in dogs

Human AD		Canine AD	
Hanifin and Rajka (1980)	Williams et al. (1994a, b)	Willemse (1986, 1988)	Prélaud et al. (1998)
Major features	*Pruritic skin*	*Major features*	*Major criteria*
Patient must have at least four of the following features:	Plus three or more of the following:	Patient must have at least three of the following features:	Patient must have at least three out of the following five features:
Pruritus	History of flexural involvement	Pruritus	Corticosteroid-sensitive pruritus
Early age of onset	History of asthma or hay fever	Typical morphology and distribution: Facial and/or digital involvement or Lichenification of the flexor surface of the tarsal joint and/or the extensor surface of the carpal joint	Erythema of pinnae
Facial and extensor involvement (children)	Generalized dry skin	Chronic or chronic-relapsing dermatitis	Bilateral cranial erythematous pododermatitis
Flexural lichenification (adults)	Onset of rash under the age of 2 years	Individual or family history of atopy, and/or breed predisposition	Cheilitis
Chronic or relapsing dermatitis	Flexural dermatitis		Appearance of first signs between the ages of 6 months and 3 years
Personal or family history of atopic disease			
Minor features		*Minor features*	
Xerosis		At least three of the following features also should be present:	
Susceptibility to cutaneous infections (*S. aureus,* herpes)		Onset of symptoms before 3 years	
Nonspecific dermatitis of the hands or feet		Facial erythema and cheilitis	
Cheilitis		Bacterial conjunctivitis	
Ichthyosis, palmar hyperlinearity, keratosis pilaris		Superficial staphylococcal pyoderma	
Pityriasis alba		Hyperhidrosis	
Nipple eczema		Immediate positive intradermal test to inhalants	
White dermatographism and delayed blanch response		Elevated serum allergen-specific IgE	
Anterior subcapsular cataracts		Elevated serum allergen-specific IgGd	
Elevated serum total IgE levels			
Positive immediate-type allergy skin tests			

were evaluated with regard to sensitivity, specificity and accuracy for diagnosis of canine AD. More recently, a list of five major criteria for canine AD was proposed by Prélaud et al. (1998), using a survey of seven veterinarians examining 96 canine patients. The presence of three out of five of these criteria in a patient resulted in diagnostic sensitivity and specificity of approximately 80% (Table 1).

Because of patient variability, such ''checklists'' of clinical criteria are not infallible, and it is important to emphasize that even a scheme that is 80% accurate will be wrong in one out of every five patients! In practical terms, if a patient meets the criteria, it is reasonable to include AD as a primary differential diagnosis, but failure to meet the criteria does not preclude the diagnosis of AD.

Regardless of the exact list of criteria used, there is general agreement that once a dog fulfills the initial clinical criteria for AD, other differential diagnoses must be ruled out. Because a major sign of AD is pruritus, and because secondary complications (such as cutaneous infections, otitis externa, and seborrhea) are both common and variable in canine AD, the list of possible differential diagnoses can be rather extensive. Additionally, a part of the clinical signs seen in a patient could be related to coexisting allergic disorders such as flea and food hypersensitivity, thus complicating diagnostic investigations. Generally, authors consider the following diagnoses to be the most important to eliminate from consideration as primary or secondary problems: flea allergy dermatitis, adverse food reactions (hypersensitivity or non-immunological reactions), scabies or other pruritic mite infestation, pruritic bacterial folliculitis, *Malassezia* dermatitis, and less commonly, cornification disorders and contact dermatitides. The reader is referred to one of the several current textbooks on veterinary dermatology for diagnostic protocols to evaluate a patient for these diseases and a general approach to the pruritic dog (Scott et al., 2000).

3. Laboratory diagnostic criteria for AD and interpretation of ''allergy tests''

Following initial clinical diagnosis of AD, one of the several diagnostic evaluations is often performed in an attempt to confirm the diagnosis with an ''allergy test.'' Typically, either a serum-based or an intradermal allergy test is conducted in canine patients. More detailed information about these tests, and in particular the objective evidence for their usefulness are provided elsewhere in this issue. However, it is important to recognize some fundamental principles about interpretation of these tests that apply no matter which method is chosen:

1. ''Allergy tests'' are perhaps poorly named, as they are not definitive tests for the presence of allergy. Allergen-specific IgE serological tests assay the presence of allergen-specific IgE in a patient; the presence and quantity of allergen-specific IgE is *sometimes*, but not always, indicative of allergy. Similarly, intradermal tests detect functional ability for cutaneous mast cells to degranulate upon exposure to allergen extracts; such reactivity is *sometimes*, but not always, indicative of allergy.
2. No allergy test is completely sensitive and specific. Clinically normal animals (and humans) can have positive reactions to such tests in the absence of clinical signs of

allergy (Codner and Lessard, 1993; Bond et al., 1994; Lian and Halliwell, 1998; Ownby, 1998). Conversely, veterinary specialists anecdotally see patients with clinical signs completely consistent with allergy, but with negative ''allergy tests''; unfortunately, such patient groups are undocumented in the veterinary literature.

3. As a consequence of the above two points, ''allergy tests'', as presently conducted, *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 and as a basis for institution of allergen avoidance measures.

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