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The ACVD task force on canine atopic dermatitis (XIII): threshold phenomenon and summation of effects

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Abstract

The concepts of a threshold for pruritus and a threshold for canine atopic dermatitis (AD) are useful in the understanding of the development of clinical manifestations of this disease. Multiple flare factors, such as infections with bacteria and yeasts, can contribute to the severity of clinical signs in affected patients.

Keywords: Atopic dermatitis; Bacteria; Yeast; Pruritus threshold

1. Introduction

The concepts of a threshold for pruritus and one for the development of atopic dermatitis (AD) in the dog are presently theoretical concepts that have not been validated or tested but are commonly used to explain the development of clinical signs. It is important to note that the concept of a threshold of pruritus is distinct from the threshold of elicitation of atopic disease. Pruritus is a separate sensation and relates to different diseases that may occur together with AD.

2. Threshold for pruritus

The concept of a threshold of pruritus relates to the presence of a multitude of stimuli (i.e. colonizing bacteria and yeast, ectoparasites, etc.) that might contribute to the level of

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itch of the individual patient. The theory of the ''pruritic threshold'' hypothesizes that any individual is able to tolerate some pruritic stimulus without becoming itchy. However, when multiple stimuli are present at the same time and they exceed the ''threshold'' of pruritus, itching will result. This is due to the summation of effects of the different diseases. In humans, the pruritic threshold is variable among individuals and may be lowered by stress (Gupta et al., 1994) and environmental factors (Gil and Sampson, 1989).

3. Threshold for AD lesions

The concept of threshold for the development of AD relates to the allergen load. At the present time no study has documented the concept of threshold for the development of AD in the dog. Patterson (1960) has shown that there is a threshold for the development of respiratory signs in the atopic dog. However, even though this concept has not been validated for dogs with AD, it is commonly accepted that in dogs with uncomplicated AD when the allergen load is low, no symptoms may be observed. In contrast, when a heavy allergen load is present, clinical disease will ensue. Alternatively there may be times of the year when the allergen-specific IgE antibody level is low and again, no symptoms of pruritus or AD will be noted. For example, a dog with both house dust mite hypersensitivity and pollen allergy may be asymptomatic during colder months (due to the lack of pollen) despite constant exposure to dust mite allergens and experience clinical disease when the pollen allergen load increases. One positive consequence of this hypothetical concept is that animals that show sensitivity to multiple allergens may be successfully managed with hyposensitization that does not include all the allergens as long as a sufficient number of clinically relevant allergens have been included in the allergy vaccine.

Dogs with AD are also at higher risk of developing other hypersensitivities including flea allergy (Halliwell et al., 1987) and food allergy (Rosser, 1993) when compared to individuals without AD. Furthermore, dogs with AD are at increased risk of developing skin infections (Bevier, 1990), possibly due to an increased bacterial adherence (McEwan, 1990). The presence of multiple allergies and the existence of secondary infections may contribute significantly to the amount of inflammation and release of pruritic mediators.

4. Discussion

Even though the threshold for the development of AD is different from the threshold of pruritus, the concept of a pruritic threshold has several important implications in the management of dogs with AD. Elimination of fleas and/or control of concurrent food hypersensitivity may cause the animal to better tolerate other offending aero-allergens. In addition, control of secondary skin infections may decrease significantly the level of discomfort of some patients (Stewart, 1988; Guillot and Bond, 1999).

It is important to note that the role of cutaneous bacteria and *Malassezia* yeast colonization in canine AD appears to be two-fold. First, they contribute to inflammation and the release of pruritic mediators (e.g. yeast contain a variety of substances that can initiate the complement cascade as reported by Belew et al., 1980). Second, they could act

as allergens against which IgE are produced. Recent studies have demonstrated that dogs with AD may exhibit positive reactions to the intradermal injection of yeast extracts and have circulating IgE against yeast antigens (Morris et al., 1998). In addition, in canine inflamed skin, the penetration of bacterial antigens appears to be increased (Mason and Lloyd, 1990) and IgE against staphylococcal antigens have been demonstrated (Morales et al., 1994). These antibodies can bind to receptors present on mast cells and basophils and induce degranulation. *Staphylococci* also contain a large number of immunologically active molecules (e.g. protein A, bacterial superantigens) that have been reported to perpetuate the atopic state in humans (Strange et al., 1996) by modulating T cell proliferation, antigen presentation, IgE synthesis and cytokine production (Herz et al., 1999; Hofer et al., 1999; Saloga and Knop, 1999).

In conclusion, it is very important to control additional hypersensitivities and address secondary infections to remove any additional stimuli and keep the patient from reaching its threshold of clinical disease.

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