

Editorial

Insights into immunoglobulin E-mediated late-phase reactions in dogs

The so-called late-phase reaction was described by Charles Blackley in the 1950s, but ~20 years earlier Stevens had reported that asthma flares usually persist for several days after allergen challenge. The late-phase reaction is usually seen after higher doses of allergen exposure in the lung, nose and eyes. It can also be produced either by the application of high doses to the target organs or by injection of allergen or anti-immunoglobulin E (IgE) reagents into the skin. Interestingly, a late asthmatic reaction can also be induced by the injection of T-cell peptides into the skin.¹ After the expected production of wheal and flare reactions, an oedematous swelling with blanching can occur ~6 h later and represents a classic cutaneous late-phase reaction. The model of cutaneous late-phase reaction has been used in a number of investigations exploring the players involved in the game of the late-phase reaction and allergy overall.

In their paper entitled 'Characterization of the inflammatory infiltrate during an IgE-mediated late phase reaction in this skin of normal and atopic dogs' by Thierry Olivry *et al.*,² the authors performed skin biopsies at several time points postchallenge in the skin of normal and atopic dogs. The authors confirmed the occurrence of the clinical signs of cutaneous late-phase reaction and described the influx of polymorphonuclear cells and thereafter mainly of T cells and dendritic cells. The changes observed were similar in atopic and nonatopic dogs, but the intensity was lower in the normal dogs, suggesting some predisposition to develop this kind of reaction in atopic individuals. This was confirmed later on by Hillier *et al.*,³ The authors emphasize the similarity of the observed phenomena to the morphological changes seen in the infiltrates of atopic dermatitis in dogs and conclude that the cutaneous late-phase reaction induced in these animals could be an excellent pharmacological model in which to investigate anti-allergic or anti-atopic pharmacological agents.⁴

It is important to highlight the artificial character of this model, because in normal clinical conditions a late-phase reaction can be induced only by an IgE-mediated challenge of the mast cells with allergens. This hardly corresponds to the reality of the skin as a target for allergic reactions provoked from external contact with allergens, where it is assumed that they should have access to the deeply localized mast cells. The clinical relevance of the late-phase reaction is documented for the airways and the eyes but is a matter of debate for the skin. With regard to atopic dermatitis, it may be relevant for some allergens able to penetrate deeply through the epidermal barrier and to have direct access to the mast cells in the dermal compartment. However, its clinical relevance for atopic dermatitis in humans, for example, has never really been shown. For obvious reasons linked to differences

between the skin of dogs and humans, allergen challenges in dogs usually need at least prick if not intracutaneous challenge,^{5,6} while in humans the epicutaneous application of clinically relevant allergens seems to be better and more relevant to atopic dermatitis.^{7,8}

Even if the cutaneous late-phase reaction in humans remains somewhat experimental in nature, it still represents an important model to understand the pathomechanisms involved in the allergen- and IgE-mediated activation of mast cells in the skin. Indeed, the role of mast cells has been tremendously revised in recent years,^{9,10} and still represents an important immunopharmacological target, which deserves our interest in the context not only of allergic but potentially also of infectious diseases.¹¹ Thus, the pioneering work of Thierry Olivry and his team in exploring the mechanisms underlying the allergic reaction induced by allergen challenge in the skin of dogs (or cats)¹² remains of importance because of the significant similarities between animals^{13–15} and humans¹⁶ with regard to allergic reactions.

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