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Allergy as an organ and a systemic disease

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Summary

Allergic disorders are viewed generally as organ diseases and thus referred to organ specialists, such as the ear, nose and throat specialist for rhinitis, the pulmonologist for asthma, the dermatologist for dermatitis, and so on. Indeed, the systemic nature of allergy is made evident by the fact that the same individual may develop during the life different manifestations to a given allergen. This is true for example in sensitisation to house dust mites, which may start in childhood as atopic dermatitis and later express as asthma or rhinitis.

The major player in driving the immune response is the T lymphocyte, and the T helper subpopulations – Th1 and Th2 – as well as the T regulatory cells, are involved in orienting tolerance or reactivity to allergens. Interesting observations on the systemic or organ-specific actions of T cells were obtained by transplantations from allergic donors to non-allergic recipients. Bone marrow is able to transfer all allergic manifestations, while lung transplantation transfers only asthma. A number of factors are involved in the expression of allergy as a systemic or organ disease and deserve deeper investigations. They include the antigen presenting cells, the homing of T cells, the cytokine and chemokine pattern, and the adhesion molecules.

Keywords: allergy, organ response, systemic response, T cells

In common medical practice, allergic disorders are viewed generally as organ diseases which may concern the nose, the lung, the eye, the skin and the gastrointestinal system. In terms of allergy management, this leads to a reliance upon organ specialists, such as the ear, nose and throat (ENT) specialist, the pulmonologist, the ophtalmologist and the gastroenterologist. Only anaphylactic reactions are considered systemic, and are thus referred to the allergist for evaluation. Indeed, the systemic nature of allergy is made evident by the fact that the same individual may encounter a number of clinical manifestations caused by the same allergic sensitization. Thus, a subject sensitized to house dust mites may begin as a child with atopic dermatitis and develop rhinitis and asthma later [1]. Another example is sensitization to pollens, expressed commonly as rhinitis and asthma but often triggering, when allergens cross-reacting with vegetables foods are involved, a spectrum of clinical reactions including oral and gastrointestinal allergy and also anaphylaxis [2].

Considering the pivotal role of T lymphocytes in regulating the immune response, investigating such cells is the most appropriate approach in understanding what influences the clinical expression of allergy as a systemic or an organ disease. Currently, we know that the response to allergens depends upon the balance between T helper type 1 (Th1) and Th2 effector cells (the latter favouring allergy), which is orchestrated by regulatory mechanisms, with an important role for forkhead box P3-positive ($FoxP3^+$) T regulatory cells [3]

Important advances in studying the systemic or organ-specific actions of T cells have been achieved in research into the effects of transplantation from allergic donors to non-allergic recipients, and vice versa. More than 20 years ago it was demonstrated that following bone marrow transplantation (BMT), non-atopic recipients developed both total and specific immunoglobulin E (IgE) comparable to the atopic donor as a result of repopulation in the recipient with IgE-specific T cells [4]. This event was confirmed in a number of investigations, and recently a follow-up study demonstrated that T and B cell clones with allergen-specific memory influencing IgE production, rhinitis and asthma extend their activity for up to 14 years after BMT [5]. Conversely, BMT from non-allergic donor to atopic recipient leads to resolution of atopic dermatitis [6]. These data indicate clearly that

BMT gives rise to both local and systemic effects on allergic disease. Other organ transplantations seem to be associated with only local effects, as reported for lung transplantation, where non-asthmatic recipients of asthmatic lungs developed asthma after transplantation while the asthmatic recipients of normal lungs no longer had asthma, thus supporting the concept of asthma as an organ disease [7] or to more complex effects. This is true for liver transplantation, with a number of reports about the development of food allergy by recipients. For some cases this was attributed to treatment with tacrolimus [8], but recently two previously non-allergic patients developing systemic reactions to foods after transplantation from a food allergic donor have been described [9]. It is possible that recipient-related factors, such as altered immunoregulatory responses, are involved in these reactions, but also that antigen-presenting cells, present abundantly in the liver, play a role in inducing an immune response to previously tolerated foods.

A factor correlated apparently with the development of a local or a systemic immune response is the route of sensitization. In an experimental model using the major birch allergen Bet v 1, the subcutaneous route was the most efficient in inducing IgE production; the aerosol route did not modify the IgE level but elicited a airway inflammation comparable to the subcutaneous route; and the intraperitoneal route had effects neither on IgE nor airway inflammation [10].

A mechanism of paramount importance to target a given organ or system is the homing of T cells. For example, in atopic dermatitis there is a subset of T cells with the ability to home to the skin by the receptor cutaneous lymphocyte antigen (CLA), which is expressed on memory T cells, and facilitates their binding to the adhesion molecule E-selectin [11].

According to Togias, the mechanisms that lead instead to the development of the systemic element probably include intricate interactions between mediators of the acute allergic reaction, locally and systemically produced cytokines and neurotrophins, the vascular epithelium and the adhesion molecule system, the chemokine network and antigen-presenting cells and their interactions with T lymphocytes [12].

The papers in this supplement deal with hypersensitivity, using the criteria of target organs to evaluate the matter but considering systemic aspects for each pathology, with the aim of providing the reader with a more complete approach to allergic diseases.

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