

Questionable coexistence of T_H1- and T_H2-related diseases

To the Editor:

During the last decade, the immune system has been described by the action of cytokines that mediate mutually antagonistic T_H1 and T_H2 immune responses. Allergic diseases (characterized by a T_H2 cytokine profile) and several autoimmune diseases (characterized by a T_H1 cytokine profile) were regarded as mutually exclusive within individuals. However, it has recently been suggested that both types of diseases are caused by immune dysregulation, allowing both T_H1 and T_H2 responses to go unimpeded. This hypothesis could explain both the simultaneous rise in insulin-dependent diabetes mellitus and allergic diseases at the population level and the shared risk factors of the 2 types of diseases. As a spin-off, it has been hypothesized that T_H1- and T_H2-related diseases are positively associated within individuals.

Very recently, 2 large register-based studies have claimed coexistence¹ (implying an association at a single point in time) and coincidence² (implying incidence at the same time) of T_H1-related diseases (such as insulin-dependent diabetes mellitus, rheumatoid arthritis, coeliac disease, and psoriasis) and T_H2-related diseases (such as asthma, eczema, and allergic rhinitis) within individuals.

The 2 studies have serious limitations. First, and most important, people with multiple diseases will be overrepresented when there is a selection from a general population into administrative data. In these studies, allergic diseases, which tend to be handled in General Practices or not at all, are likely to be diagnosed and registered more readily in patients with autoimmune diseases. This could lead to a considerable overestimation of the association between the 2 types of diseases.

Second, both studies have weaknesses with respect to the diagnosis of allergic diseases. The study by Kero et al¹ includes data on hospitalizations and data on medication. As shown previously by the authors, there is little overlap between the 2 groups.³ Thus the asthma diagnosis is likely to include, to a large extent, hospitalizations in the first years of life that are caused by respiratory infections, which in most cases have nothing to do with T_H2-related atopic asthma—but might be more common among children with chronic diseases. In the study by Simpson et al,² the observed association of T_H1- and T_H2-related diseases was founded on an association between psoriasis and “eczema.” Psoriasis is most common in adulthood, when atopic dermatitis is rare, and the diagnosis “eczema” is likely to include a variety of skin conditions that have nothing to do with T_H2-related atopic dermatitis. Accordingly, in this study it is also questionable whether the observed association can be considered to be between T_H1- and T_H2-related diseases. Even if the diagnoses were correct, the analysis would at best prove coexistence, not coincidence.

We agree that the simultaneous rise in several T_H1- and T_H2-related diseases at the population level supports a common etiology. However, this does not necessarily imply that the 2 types of diseases are likely to exist at the same time in the same individual. Most studies support an inverse association between T_H1- and T_H2-related diseases within individuals. Therefore, on the basis of the existing material, we find no evidence for either coincidence or coexistence of T_H1- and T_H2-related diseases.

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