Bronchial Asthma – An Immunologic Disease

Bronchial asthma (BA) represents the manifestation of allergic diseases on the airways and the lung. The disease is characterized by a certain type of airway mucosa inflammation and the presence of a state of increased airways responsiveness (AR). AR is defined as an abnormal response of airway smooth muscle cells to a variety of stimuli including allergens, air pollutants and pharmacological agents such as histamine and metacholine [1, 2]. Local exposure to these stimuli causes narrowing of the airways at a dose and concentration range which usually is uneffective in nonasthmatic subjects. The results from numerous family studies indicate that genetic factors contribute to the development of BA.

These and other data provide evidence that the development of BA is the result of a complex interplay involving several levels of regulation. A still undefined genotype represents one important prerequisite for the development of the disease. Allergic sensitization can occur on the basis of this genetic background. Allergic sensitization also depends on local exposure to the respective allergens. Once allergic sensitization is fully established, an asthmatic attack is triggered by local challenge with the relevant allergen or other nonspecific stimuli. Therefore, the clinical manifestation of the disease is the result of the combination of genetic background, allergic sensitization and local exposure to trigger factors and allergens [3–7].

Central to the understanding of the pathogenesis of BA is the analysis of the mechanisms resulting in allergic sensitization (Fig. 1), which requires the interaction of several cellular components of the immune system. This process is initiated by antigen-presenting cells (APCs). Each compartment of the immune system hosts more or less specialized APCs. In the lung, alveolar macrophages function as APCs as do dendritic cells in local draining lymph nodes. APCs phagocytose and process allergens and, as a result of allergen processing, they present small allergenic peptides on MHC class II molecules. Presentation of allergenic peptides requires the presence of defined MHC class II molecules. Several groups have clearly demonstrated that there exists a linkage between the expression of certain HLA-DR antigens and the development of an allergic sensitization which results in the production of allergen-specific IgE antibodies [8–10]. Some MHC class
II molecules present specific peptides better than others. For example, sensitization to house dust mite allergens was associated with the expression of certain HLA-DRB3 gene products [11]. In addition, the same HLA-DR product was detected in increased frequency among patients allergic to birch pollen allergen. In contrast, a different HLA-DR allele, HLA-DRB1, was associated with sensitizations to cat allergen Fel d I.

MHC class II molecules present peptides to CD4+ T cells, which recognize this complex using their T cell receptor (TCR). Each T cell expresses its unique TCR on the cell surface. The majority of T cells express a TCR which consists of one α and one β chain. Each chain bears several different elements, e.g., variable elements Va and Vβ. The composition of the TCR results from a complex rearrangement of TCR genes which occurs in the thymus and shapes the individual TCR repertoire. The composition of the TCR elements defines the antigen/allergen specificity of a T cell. Recently, increasing number of allergens were cloned and sequenced. Based on the analysis of these proteins, studies were designed to identify amino acid sequences that are presented as peptides on MHC class II molecules and recognized by the TCR of CD4+ T cells. For example, the analysis of T cell clones reactive to the house dust mite allergen Der p 1 indicates that the epitopes 45–73, 89–117 and 111–139 were preferentially recognized by these clones [11]; however, not all T cells from different allergic patients recognize the same peptides. It seems to be that each individual has his/her own panel of peptides that is recognized by T cells. The genetic basis of this phenomenon is not fully understood. The MHC class II repertoire expressed on APCs, the TCR repertoire used by T cells of the allergic patient and the