EDITORIAL

BRONCHIAL SMOOTH MUSCLE REEVALUATED

From the definition of asthma as "a disease characterized by wide variations, in short periods of time, of resistance to airway flow" (1) in 1959 to the current concept that "asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a major role" (2), considerable progress has been made in our knowledge of the elements implicated in the onset and progression of the disease.

Once the participation of the autonomic, adrenergic and cholinergic systems in the maintenance of bronchial caliber through specific receptors for the respective neurotransmitters situated in the smooth muscle membrane became known, the pathogenesis of asthma centered on a possible imbalance between both neurological systems due to alterations in the β_2-adrenergic receptors with a consequent predominance of constrictive cholinergic action. With regard to this supposition, Szentivanyi's beta adrenergic theory enjoyed a certain notoriety. This theory hypothesized various alterations in the number or action of these receptors, which would explain hyperirritability or hyperreactivity *(3).*

For some time, bronchial hyperreactivity, or bronchial lability, was considered to be the basis of the pathogenesis of asthma although the mechanisms were not sufficiently clear. However, the hypothesis of bronchial inflammation as the main cause of the disease and, above all, of its chronic nature soon began to gain ground and was subsequently widely accepted. The role of various cells and their mediators in the inflammatory reaction became known. The cells responsible for this reaction are mainly eosinophils and mast cells, which characterize allergic inflammation.

Inflammation leads to lesions of the bronchial mucosa that leave vagal nerve endings exposed. Stimulation of these nerve endings by various substances or allergens lies at the origin of the bronchoconstrictor reflex (4). Hence, the deduction that bronchial hyperreactivity was secondary to inflammation was made and inflammation consequently came to occupy a preeminent position in the etiopathogenesis of asthma. From this it can be deduced that the main treatment of asthma consists of corticosteroids, especially inhaled corticosteroids. This widely used treatment has undoubtedly played a major role in the improved course and prognosis of the disease.

Evidently, hyperreactivity can exist without inflammation just as inflammation can exist without hyperreactivity (5, 6). Many children who have close relatives with atopic asthma experience their first dyspnea crisis in the first few months of life without having suf-

fered from a viral infection (especially respiratory syncytial virus). This suggests the existence of primary bronchial hyperreactivity as well as a possible atopic predisposition.

The identification of a gene related to the β_2-adrenergic receptor on chromosome 5q31 and the subsequent identification of specific mutations in the codon codifying this receptor support the existence of congenital bronchial hyperreactivity and some of these mutations have been related to the severity of asthma (7).

The major role played by mast cells in asthma, even in non-atopic asthma, is well known (8, 9). In addition to histamine and other mediators that provoke smooth muscle constriction, other mediators attract the cells provoking the inflammatory reaction (eosinophils, neutrophils). Therefore, mast cells contribute to both smooth muscle constriction and inflammation (10, 11). These cells are known to be situated in the bronchial submucosa and a recent study has revealed that they are also situated in smooth muscle and are found in a higher proportion in asthmatic patients than in healthy controls or in patients with eosinophilic bronchitis, which does not provoke bronchospasm. Furthermore, the higher intensity of hyperreactivity, evaluated by the response to inhaled methacholine, seems to be related to the higher concentration of mast cells (12).

It remains to be demonstrated whether this higher concentration of mast cells in smooth muscle cells is compatible with the greater secretion in asthmatics of a known factor that regulates mast cell growth, function and survival, and which is found within the bronchial smooth muscle layer (13, 14).

Lastly, a recently published experimental study has reported changes (15) in the sensitivity of smooth muscle as a consequence of T lymphocyte-induced IL-5 and IL1β release, thus demonstrating once again the preeminent role of smooth muscle in the pathogenesis of bronchoconstriction (16).

Without minimizing the undoubted importance of the inflammatory reaction in airway flow reduction, the studies discussed above give smooth muscle pride of place in the pathogenesis of asthma, a finding that has therapeutic implications for the future (11, 17, 18).

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