EDITORIAL

VALIDITY OF THE HYGIENE HYPOTHESIS

It is well known that the prevalence of allergic diseases has markedly increased in the last few years, especially in high-income countries and urban areas. Consequently, the improved hygienic conditions in these environments have been related to an immune response imbalance, once the subsets of T helper lymphocytes became known – Th1 being more closely related to defense against infection and Th2 being involved in allergic reactions[1]. Previously, Strachan (1989) had formulated what is known as the «hygiene hypothesis», according to which infection in early childhood – transmitted through unhygienic contact with siblings or acquired prenatally through the mother being infected by contact with her older children – may prevent the development of allergic diseases[2]. This hypothesis was subsequently bolstered when the immunomodulatory capacity of some bacterial antigens and repeat infections was identified; this phenomenon stimulates the predominance of a Th1 over a Th2 cytokine profile, thus hampering allergen sensitization. In short, the improved hygiene among the general population is believed to produce a Th1/Th2 imbalance, with a predominance of Th2 lymphocyte activity, and a consequent shift toward a Th2 immune response.

The hygiene hypothesis seems to be confirmed by the role of endotoxin content in the home. Endotoxins are lipoproteins associated with the outer membrane of Gram-negative bacteria and behave as highly potent immunomodulators. On monocytes, macrophages and dendritic cells, endotoxins induce IL-12 production, activating Th0 cells to differentiate into Th-1 lymphocytes, which produce IFNγ; both cytokines inhibit the production of Th2-associated interleukins[3,4].

Epidemiological studies have revealed the low prevalence of allergic rhinitis and asthma due to aeroallergen sensitization in persons growing up in environments with elevated endotoxin concentrations; in contrast, exposure to endotoxins at a later age gives rise to allergic disease, especially in atopic individuals; if these individuals already have a disease of this type, it will be aggravated by endotoxin inhalation. This apparently paradoxical response to endotoxin exposure is due to distinct circumstances, such as the moment and duration of exposure, the quantity of endotoxins in the environment, the presence of environmental cofactors (other potentiating bacterial components have been detected), and a genetic predisposition to atopy[5].

Although the hygiene hypothesis was initially received with skepticism – with no lack of critics casting doubt on it[6] – its credibility has increased, especially as the mechanisms through which the immune response tends to show a Th2 pattern in certain circumstances has become known, giving rise to the recent proliferation of studies designed to elucidate these phenomena[7,8,9].

In this issue of Allergologia et Immunopathologia, *an update on the mechanisms of inflammation in allergic diseases by Montero[10] mentions the role of regulatory T lymphocytes (Treg), which have recently been identified[11], and their possible involvement in the regulation of immune response against endogenous gastrointestinal microbiota, which could be an important mechanism in Th1/Th2 imbalance[12].*

The possibility that other mechanisms play a role in this imbalance has not been ruled out; these mechanisms involve antigen-presenting cells (macrophages and dendritic cells), in which there are several known receptors such as Toll-like receptors (TLR), which play a crucial role in bacterial antigen recognition. TLR4 and TLR9 – and especially TLR2 – seem to be the main receptors involved in recognition of the components of the cell membrane of environmental saprophites[7,13].

In summary, the hygiene hypothesis is based not only on clinical observations and studies of the prevalence of allergic diseases in various hygienic-environmental conditions, but also finds solid support in the identification of mechanisms that may play a role in lymphocyte function imbalance.

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