

## **Air Pollution, Climate Change and Hygiene Hypothesis**

To be allergic we must have a genetic make-up that predisposes us to allergy and we have to be exposed to the adequate environmental stimuli. Then, the increased allergy prevalence must be caused by a change in either our genetic predisposition or in the environmental allergenic stimuli. It is clear that only extremely powerful external stimuli could induce acute genetic changes immediately visible in the same or in the next generation. Therefore, genetic changes cannot be the cause of the increment of allergy prevalence. On the contrary we have suffered a tremendous change in our way of living. Up to hundred years ago we had a pre-industrial life style that was rural with most outdoor activities; the occupational practices were farming and agriculture with close contact with stock, farm products and higher rate of infections due to the poor hygiene.

In the last century our life style became more urban with mostly indoor activities and higher level of hygiene. This century of hygienic improvement reduced the rate of infections but increased the atmospheric pollution, the global temperature and stress.

In 1989 D.P. Strachan, suggested by the first time the hygiene hypothesis and wrote that "infection in early childhood, transmitted by unhygienic contact with older siblings or acquired prenatal from a mother infected by contact with her older children might prevent the development of allergic illnesses". A large number of population-based studies have since confirmed the inverse association between the number of siblings and the development of allergic outcomes. Later, Erika Von Mutius made three distinct claims on the proper nature of the hygiene hypothesis: a) Overt and unapparent infections of human subjects with viruses and bacteria may decrease the risk of developing allergic illnesses; b) Non-invasive microbial exposures in the environment may decrease the risk of allergies and c) Both of these exposures, be it infections or non-invasive microbial exposures, may influence a subject's innate and adaptive immune response. She also explained that are four conditioning factors hygiene hypothesis: the different allergic illnesses and phenotypes; the timing of the exposure; subject's genetic susceptibility and the various environmental exposures.

In the 90s, Sergio Romagnani, gave a giant step in the knowledge of the immune system, describing the Th1/Th2 paradigm and the importance of a balanced immune Th1/Th2 response. Then, it was demonstrate the importance of Th2 pattern in the development of the allergic sensitisation. Every single immunological problem was explained with the Th1/Th2 paradigm but still some problems remained without a convincing explanation. For instance, among kids in various studies in different areas of the world around 30% have antibodies against dust mite allergen (suggesting they all are exposed) but whereas asthma is found in 12% of kids from Europe and Australia, only 3% have asthma in Gambia and Nigeria. Then, at late 90s, many scientific groups started to describe a new group of T cells with capacity to expand or inhibit the different immune response known as T regulatory cells. The main families of T reg cells described were: -CD4+ Th2, -CD4+ Th3 cells, -CD4+ Tr1 cells, -CD4+ CD25+ T cells and -CD8+ Tr cells. Many potential therapeutic possibilities of T reg cells were suggested. Also the role of IL10+CD4+CD25+ T cells in the immunotherapy. The concept of Th1/Th2 balance was substituted by a new concept, the balance between allergen specific T regulatory cells and T helper cells. But still we were not able to explain all immunological problems.

In 1998, a homologous family of toll receptors, termed toll-like receptors (TLRs) was found in vertebrates. These receptors recognize pathogen associated molecular patterns (PAMPs) that are shared by many pathogens and are conserved microbial molecules.

The stimulation of TLR signalling regulates the development of Th1 and Th2 cells. TLR stimulation by PAMPs induces the development of a Th1 response and protects the development of allergy sensitisation. New studies of Sergio Romagnani demonstrate how a missing immune deviation through TLR is the cause of an increase of Th2 cells and consequent allergy profile. In other words, in the absence of Th1 polarizing stimuli mucosal immune responses fail to overcome their inherent Th2 bias and become skewed in the direction of allergy.