

Microbiome and allergic airway disease: A critical window in early life

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Allergy often occurs in genetically predisposed individuals but an interplay with an altered immune system, environmental triggers /allergens leading to chronic inflammation are among the key factors. Among the factors that have led to rise of allergic diseases are the rapid urbanization, change of lifestyle and changes in the environment and reduction in exposure to microbes in early life.

Reduced biodiversity and climate change has been shown to have an adverse impact on human health. However, less attention is given to the effects of reduced biodiversity on the loss on environmental and commensal microbiotas. Commensals are active and essential participants in the development and maintenance of barrier function and immunological tolerance. They are also involved in the programming of many aspects of T cell differentiation in co-operation with the host genome. Studies of healthy individuals and those with disease reveal that reduced biodiversity and changes in the composition of the gut microbiota are associated with a variety of chronic inflammatory diseases like asthma, type I diabetes, inflammatory bowel diseases and obesity. All these inflammatory diseases have shown an increase in prevalence during the past few decades in both developed and developing countries. These alterations in indigenous microbiota and the lack of general microbiota are characteristically associated with the changing life styles towards urbanization. These act as key risk factors for immune dysregulation and impaired tolerance. The risk is further enhanced by lack of exercise and altered dietary habits. Studies done involving immigrants moving from developing countries to more developed countries have suggested that tolerance mechanisms can rapidly become impaired in microbe-poor environments.

Most of the current literature have largely described about the gut microbiota. However, more recent metagenomic studies demonstrate a significant role for microbiotas also in the respiratory tract and skin. These play a crucial role in regulating the immune cells that are of relevance to asthma and allergic diseases, such as Th1, Th2, Th17, Treg and dendritic cells as well as Toll-like receptors. Healthy adults

have been shown to harbor significantly more species-rich and diverse nares microbiotas than do hospitalized individuals. Approximately twice as many species-level microbial groups have been identified in healthy adult nares microbiotas as those found in inpatient microbiotas. Some studies have shown a close relationship between CRS and *Staphylococcus aureus*, anaerobes and so on in the nasal cavity or paranasal sinuses, although the relationship between CRS and microorganisms in the gut has not been demonstrated. The relationship between asthma and CRS has been clearly shown, and in particular, CRS with nasal polyps (CRSwNP) considered to be Th2-dominant. Studies examining environmental microbial exposure in populations at risk for CRS are necessary to improve our understanding of the role this factor plays in disease development. Moreover, the link between lung microbiota and the gut, has also been unraveled and the association with respiratory diseases such as asthma diseases onset, severity and progression have been shown.

Microbiota in early life can influence the development of inflammatory diseases like asthma, AR and CRS and therefore a critical window for potential intervention. Knowledge of the diverse multisystem effects has given rise to strategies that are being considered to favourably modulate the gut microbiota. A recently published guideline by the WAO the GLAD-P recommends specific preventive interventions such as dietary supplementation - based on a systematic review of evidence.