Editorial to the special issue "Environmental influences on childhood asthma"

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Back in 1892, Sir William Osler gave an accurate description of asthma as a disease that is associated with "spasm of the bronchial muscles, inflammation of the smaller bronchioles, bizarre and extraordinary variety of circumstances and cold infections, often running in families (1,2). This is basically a true reflection of our modern understanding of asthma which states that asthma is a complex genetic disorder that involves interactions between genetic and environmental factors.

Since the human genetic makeup has not changed significantly in the last couple of decades, there is reason to believe that the overall increase in asthma prevalence (3) can be attributed to the changing environmental conditions of modern life. The role of environment in asthma is not limited to its role in the pathogenesis of the disease. Since it is currently not possible to change the genetic make-up of an individual underlying a complex genetic disorder such as asthma, modification of environmental conditions emerges as a significant tool for its treatment. Therefore, understanding the environmental factors that play an important role in asthma is crucial in understanding the disease pathogenesis as well as modification of factors that modulate the inception and progress of the disease as well as its treatment.

Various studies published in the last years in the journal and included in this virtual issue have addressed these questions. Garcia-Serna et al. have found out that gestational exposure to traffic-related air pollutants (TRAP) may increase the pro-inflammatory and Th2-related cytokines in newborns which might influence immune system responses later in life (4). Similarly, Pesce et al. (5) have investigated the association between prenatal exposures to heavy metals and atopic diseases. The serum concentrations of lead, cadmium and manganese were assessed in maternal blood samples collected during pregnancy and in cord blood of 651 mother-children pairs. The authors have concluded that the levels of cadmium in cord blood were associated with greater risk of asthma at the age of 8. Baek et al. have documented that exposure to phthalates are associated with airway dysfunction in childhood and this effect was partially attributable to increased serum periostin levels (6). Regarding the association between the genes and environment, Theodorou et al. (7) have investigated the role of mitogen-activated protein kinase (MAPK) pathway in 232 children who were selected from two cross-sectional cohorts and one birth cohort study. They have isolated peripheral blood mononuclear cells (PBMC) from children with asthma along with healthy controls and stimulated them with farm-dust extracts or lipopolysaccharide. The results have shown that the children with asthma have expressed significantly less dual-specificity phosphatase-1 (DUSP1) which is the negative regulator of MAPK pathway. They have conclusively indicated the possible role of DUSP1 for future therapeutical interventions regarding the anti-inflammatory features of farming environments.

In an effort to further elucidate the environmental factors that are central to our understanding of asthma, the journal has started a review series to provide a comprehensive picture on the role of environment on various aspect of asthma. Major subheadings included

1. Biodiversity
2. Urban exposures
3. Gene-environment interactions
4. Farm effect
5. Air pollution
6. Climate change
7. Allergens
8. Diet microbiome and obesity

In the virtual issue of the journal Tari Haahtela (8) has focused on the effect of biodiversity. Evidence supports that the immunomodulating roles of different micro-organisms may be protective for asthma and allergic diseases. The studies from the neighboring Finnish and Russian Karelia regions, which the author named as "the living laboratory", have shown strong evidence for the central role of environment and lifestyle which modify the human microbiome, immune balance, and thus allergy and asthma risk. Diversity of the human microbiome as well as the diversity of the natural environment that we live in and more contact with the nature are important determinants of physical health.

Grant et al. (9) have focused on the influence of urban exposures on childhood asthma. The authors have meticulously summarized and analyzed the results of previous studies which aimed to investigate the interaction between indoor allergens, microbes, indoor and outdoor pollutants, social determinants and childhood asthma along with the opportunities for intervention. Multiple environmental exposures and influences contribute to the increased incidence of asthma and excess asthma morbidity among children with asthma living in urban communities. Indoor pest allergen and mold exposures have been repeatedly linked to increased asthma diagnosis, symptoms, and exacerbations in urban children. However, studies in high-risk urban populations also found that early life pest allergen exposure, along with microbial and endotoxin exposure may be associated with a decreased risk of wheezing and asthma suggesting that the association is more complex than previously thought.

Since asthma prevalence varies widely depending on the socio-economical level, changes to help reduce inequities and inequalities in social determinants of health such as poverty, housing disrepair, higher rates of obesity, and chronic stress may produce positive effects at the population-level.

Hernandez-Pacheco et al (10) have reviewed the latest gene-environment interaction (GxE) studies in childhood asthma. They have summarized the role of various environmental exposures and the current state of knowledge on asthma genetics. The field of GxE in asthma has drastically evolved together with technological advances over the last years. However, despite reports on the effect of numerous environmental factors on childhood asthma, the availability of detailed and diverse exposure data is limited. Tobacco smoke remains to be the most accessible and extensively explored factor followed by traffic-related air pollution in GxE studies.

Airway epithelium seems to be central in gene-environment interactions. The effect of the exposure to certain environmental factors early in life on the modification of the risk and severity of asthma later in childhood is partially dependent on the functionality and integrity of the airway epithelium. It is known that the environmental exposures can trigger an inflammatory response and the disruption of the barrier and mucociliary function.

Although there are several methodological and conceptual challenges with GxE interaction studies, recent data have led to new insights into childhood asthma pathophysiology which is best exemplified by the 17q12-21 asthma locus. Some of the SNPs at this locus seem to be associated with the onset of childhood asthma, thereby highlighting the importance of age related factors in gene environment interactions.

The need for longitudinal and functional studies which provide insights into the biological mechanisms underlying the observed associations between environmental exposures and epigenetic changes that modify the asthma risk is highlighted.

Another extensively studied environmental factor that is associated with childhood as is the so called "farm effect". Frei et al. (11) have summarized the current knowledge on how "farm effect" influences the immune homeostasis during the intrauterine period and in childhood with a focus on immune mechanisms induced by environmental microbial diversity and microbial components. Farming lifestyle factors including nutrition influence the immune homeostasis either by regulating the innate immune system or by induction of regulatory T cells or TH1. We see diversity as a significant factor also in the farm effect. Diversity of environmental microbes, the diversity of the gut microbiome, or the diversity of the nutrition emerge as significant factors.

Paciencia et al. (12) investigated the association and mechanisms between air pollution and asthma in children along with the precautions that should be taken to reduce the burden of air pollution on asthma. Environmental conditions are not shared equally across the populations, regions, and settings where people live, work, and spend their time. Urban conditions and air quality are not only important features for national and local authorities to shape healthy cities and protect their citizens from environmental and health risks, but they also provide opportunities to mitigate inequalities in the most deprived areas where the environmental burden is highest. Actions to avoid exposure to indoor and outdoor air pollutants should be complementary at different levels –individual, local, and national levels – to take strong measures to protect children.

Taken together, these reviews provide a very comprehensive coverage on the role of environmental factors on childhood asthma and suggest that efforts to modify these factors may have beneficial effects not only on the individual level but also at the population level.

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CONFLICT OF INTEREST

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