Korean Cohort for Childhood Asthma and Allergic Diseases

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Allergic diseases including asthma, atopic dermatitis, and allergic rhinitis are one of the most common chronic childhood diseases with dramatic increases according to time changes and affect costs more to manage than ever before. Recently, DOHaD hypothesis proposed that all organ systems undergo developmental programming in utero that predetermines subsequent physiologic and metabolic adaptations during adult life. Especially, in allergic disease, genetic background and environmental exposures during in utero and early infant period play major roles in the development of allergic diseases. We proposed cohort studies to stress the importance of evaluating the identification of environmental factors and/or genetic factors on the development of allergic diseases during critical time windows and the natural course of allergic diseases. Further, we expect these investigations can provide a new approach for the prevention and treatment of allergic diseases.

COCOA (Cohort for Childhood Origin of Asthma and Allergic Diseases) Study

The Cohort for Childhood Origin of Asthma and Allergic diseases (COCOA) is an ongoing prospective birth cohort study, designed to investigate the effects of prenatal and early infant’s environment and genetic factors on the development of immune system, allergic diseases and children’s health. This observational prospective study, which commenced in November 2007, included pregnant women from 25 weeks of gestations from 4 medical centers in Seoul (Asan Medical Center, Samsung Medical Center, Severance Hospital, and CHA Medical Center) and is following their offsprings from birth through age 20.

Questionnaires were designed to assess health conditions, mental health, diet, and environmental factors. Regular follow-up visit was conducted as scheduled starting at 36 week of gestation and at birth, one month and 6 months, then yearly from 1 year to 6 years etc. In addition, blood samples and home environment at each period from mother, father and child were taken for the analysis. Skin prick test and impulse oscillometry and fractions of exhaled nitric oxide were measured according to specific age. Thus far, about 1600 women and infants were recruited in this prospective study, which will be followed up until 2018.

From COCOA birth cohort study, we found that cord blood mononuclear cells proliferative response to
Phytohemagglutinin stimulation may predict the development of atopic dermatitis (AD) at 12 months of age. In addition, prenatal home renovation during pregnancy was significantly associated with elevation of cord blood IgE levels and atopic dermatitis in early life, especially in infants with atopic mothers. Also, Caesarean section delivery is a risk factor for the development of AD in susceptible infants with a parental history of allergic diseases, which is modified by IL-13 and CD14 polymorphisms. Also, we found that a maternal history of allergic diseases might be associated with child’s birth weight.

The ongoing COCOA birth cohort study will reveal useful information concerning the effect of environmental factors on the development of allergic diseases and the interaction between environmental factors and genetic factors in the development of allergic diseases.

**CHEER (Children’s HEalth and Environmental Research) Study**

Children are more vulnerable to the hazards of environmental factors than adults, and these factors may influence human health later. Only a few studies in Korea thus far have reported the effects of pollutants on children’s health. To control environmental diseases and enable relevant policy implementation by the government, assessment of environmental effects and health risk resulting from these environmental pollutants is crucial. CHEER study aimed at elucidating the effect of exposure to environmental toxic substances including air pollution, heavy metals and tobacco smoke etc on child’s health; the proposed hypothesis was that toxic materials in the environment can cause environmental diseases such as cancers, neurobehavioral diseases, respiratory diseases, and allergic diseases. In this study, we aimed at determining the degree of exposure to toxic substances and estimating the contribution of environmental pollutants to the incidence and prevalence of allergic diseases in children.

Our study was performed from 2005 to 2010, and enrolled approximately 7,050 elementary school students aged below 10 years as a nation-wide prospective study, from 33 elementary schools in 10 areas of Korea. We measured the levels of toxic substances including heavy metals (lead and mercury), endocrine disrupting chemicals, and specific biomarkers. With regard to allergic diseases, we assessed lung function with spirometry and airway hyperresponsiveness with the methacholine challenge test, in addition to measuring the and IgE concentration and skin prick test. Further, we followed one-fourth of the participants from the first or second grade to 5th or 6th grade of elementary school children in 2 more consecutive periods biennially during the 6-years study period.

We determined the current degree of exposure to environmental toxic substances, the prevalence and incidence of allergic diseases such as allergic diseases, annual trends of degree of exposure to toxic materials, and the relationship between environmental toxic substances and allergic diseases. The results of this study can be utilized as basic data to control the levels of pollutants harming children’s health, especially those causing allergic diseases.

From this study, we found that ozone exposure was significantly associated with the 12-month prevalence of wheeze (odds ratio per 5 ppb, 1.372; 95% confidence interval, 1.016-1.852). Ozone was also associated with allergic rhinitis in children who reside in industrial areas. In addition, significant positive associations between ozone and the rate of newly developed sensitization to outdoor allergen were found. Also, ozone exposure and bronchiolitis history synergizes to increase the risk for current wheeze, new development of wheeze and bronchial hyperresponsiveness. In addition, we analyzed the cluster analysis from this cohort, then we extracted four clusters in childhood mild asthmatics. Atopy, gender, bronchial hyperresponsiveness and BMI are important factors to
determine the subtypes and prognosis of mild asthma in childhood. Bronchial hyperresponsiveness is sustained in atopic asthma phenotypes but the symptom prevalence decrease in the same clusters with aging.10)

**KOREA (Korean Childhood Cohort from Early Recurrent Wheezing to Asthma) Study**

In addition, we also built up KOREA cohort study which investigates to define the natural course of children with recurrent wheezing to asthma in preschool children since 2009. In future, we hope to define accurate phenotype of preschool child’s asthma, natural course and prevention method.

In summary, through our cohort study, we hope to demonstrate a causal relationship between environmental factors and development of allergic diseases and investigate gene–environment interactions in the origin of allergic diseases. In addition, we will find most appropriate target and method to prevent or modulate the development of allergic diseases from our cohort study.

**References**
