AllerGen

CHILD Study

BACKGROUNDER

CANADIAN HEALTHY INFANT LONGITUDINAL DEVELOPMENT (CHILD) STUDY

LEGACY PROJECT

Research Leader: Dr. Malcolm Sears

OBJECTIVE

The CHILD Study was developed by an academic consortium of over 40 world-renowned Canadian researchers and physicians initiating a birth cohort study of the early-life origins and development of asthma, allergies, and other chronic immune/inflammatory diseases. The CHILD Study will reveal, in unprecedented fashion, root causes (genetic, environmental and psychosocial) of allergic disease and asthma, enabling short- and long-term novel preventive strategies, evidence-based public policy and improved disease management.

The biological and epidemiological data collected by the CHILD Study includes: genetics and epigenetics, environmental exposures (including diet, nutrition, air quality, viral infections and psychosocial factors), gene-environment interactions, and immunological and health outcomes. Not only does the CHILD Study offer inroads toward modifying the severity and type of allergic diseases and asthma, it also establishes a robust database gathered from a diverse multi-generational population that can facilitate major advances in other areas of medicine, including those focusing on dermatological, neurological, cardiovascular, gastrointestinal and pulmonary diseases.

The CHILD Study also constitutes a focal point for numerous other research studies undertaken by Canadian investigators within AllerGen and across Canada. The CHILD Study has stimulated the formation of cross programmatic studies and scientific research platforms that have catalyzed networking across the country. These include task-specific CHILD working groups in immunology, psychosocial factors, infant pulmonary function, environmental exposures, genetics, clinical assessment, biomarkers, and biological sample banking.

The CHILD Study has also established links with other birth cohort studies. It is harmonizing data and analyses from two initiatives led by Dr. S. Anand: the South Asian Birth Cohort (START), which aims to recruit 1,000 pregnant women and follow the mother-child dyad prospectively for a minimum of three years to determine the genetic and environmental determinants of adiposity and related metabolic parameters, and the Aboriginal Birth Cohort (ABC), in which Aboriginal mothers and their offspring are being recruited from the Six Nations reserve near Brantford, Ontario. Discussions continue regarding other potential collaborations with international cohorts.

NEED FOR RESEARCH

Allergy and asthma are major causes of morbidity and mortality in Canadian children and Canada is near the top of the list of industrialized countries facing a growing prevalence of allergies, such as asthma, hay fever, eczema, and food and pet allergies. The related healthcare and socio-economic costs, and potential impact on the next generation, are enormous.

This made-in-Canada national, population-based, longitudinal birth cohort study provides an optimal setting for study of the multiple, interrelated, time-dependent determinants of allergy and asthma: it will provide the knowledge needed to determine how to reduce the prevalence and impact of these diseases.

RESULTS SO FAR

The CHILD Study has recruited 3,629 pregnant women (most with fathers/partners) and their babies, representing over 10,000 Canadians. The current attrition rate is approximately 5%. The data are statistically sufficient to facilitate multiple research findings. For instance, preliminary findings suggest mold was present in 40% of homes examined. Urine analyses indicated exposure to phthalate was attributable to household substances. Within their first year, over 10% of children had experienced recurrent wheezing; 16% had one or more positive skin allergy test results; 14% had atopic dermatitis; and 6% reported a food allergy. Almost all children have completed the one-year assessment and many are now completing their three-year visits.

CHILD Clinical Sub-Studies

Pulmonary Function and Respiratory Tract Infections (Toronto cohort)

Children with persistent asthma have evidence of fixed airway dysfunction by age six. However, the underlying pattern of airway dysfunction development and its causes are unknown. In the Toronto cohort at The Hospital for Sick Children, infant pulmonary function is being measured in a portion of the study population, using state-of-the-art methods (*e.g.* raised volume rapid thoraco-abdominal compression, multiple breath washout, tidal breathing exhaled nitric oxide). Infant lung function is assessed at three months, one and two years. Spirometry and multiple breath washouts will be measured annually at three, four and five years. Preschool spirometry has been proposed for the entire cohort at ages three and five. Trajectories established in the Toronto cohort may be applied to the national cohort, which will maximize usability of data to examine factors involved in the development of asthma.

Sleep (Edmonton cohort)

Childhood Sleep Disordered Breathing (SDB) is associated with poor school performance and Attention Deficit Hyperactivity Disorder (ADHD). SDB is common in childhood; one study found 60% of 6,800 pre-school children reported snoring in the previous year, 8% were habitual snorers (snored more than three nights a week) and 1% were habitual snorers with significant sleep disturbance. SDB is more common among children with allergic rhinitis and asthma, and worsens when they suffer viral respiratory tract infections and exacerbations of allergic rhinitis. CHILD is the first birth cohort study to use objective measures of sleep in children under five years of age. This sub-study will test hypotheses related to childhood SDB and outcomes such as neurodevelopment and cardiovascular disease (*e.g*. hypertension). In addition, sleep disruption and SDB may be an important confounder in determining asthma severity among the CHILD Study participants.

Perfluorinated Compounds (Winnipeg cohort)

Perfluorinated compounds are ubiquitous in our environment. They are found in everything from stain repellants to non-stick coatings, “Gortex’-type fabrics, computer and camera parts, and a wide range of foodstuffs. They can be ingested or absorbed by contact, and in various states they are volatile and can be inhaled. They have the appearance of short-chain fatty acids and can be incorporated into cell walls. Some data show changes in immunoglobulins with high level exposure and a murine model developed by this team shows pulmonary function changes. This sub-study is analyzing exposure in the home and correlating exposure with wheezing syndromes in early life as part of the CHILD Study.

Microbiome Research

Infant intestinal microbiota play a crucial role in the maturation of the immune system. Alteration of microbiota during early life has the potential to cause disease later in childhood, as evidenced by reduced levels of bifidobacteria and increased levels of *C. difficile* in the microbiota of infants who develop atopic disease (allergy and asthma) as children. Understanding the environmental determinants of infant microbiota is an important priority in child health research. Two research teams are using CHILD fecal samples and clinical and immunological data to investigate the role of the infant microbiome in health and disease.

Chemical Management Plan (CMP): Phthalate Exposures in Canadian Children During the First Three Years of Life

Environmental exposure to substances such as phthalate plasticizers during fetal development and infancy may play an important role in the development of asthma in Canadians. These studies expand upon previous phthalate exposure work conducted by AllerGen investigators, funded by Health Canada, to better understand the effects of early life exposure to indoor and outdoor air pollution. Current research findings are providing longitudinal estimates of exposure to these contaminants in young children, from three months to three years of age, through the analysis of data and information obtained as part of the CHILD Study. Research questions focus on bio-monitoring and exposure surveys made at 12, 18, 24, 30 and 36 months of age. Urinary biomarkers have been analyzed for levels of phthalate metabolites and will be correlated with consequent respiratory health effects.