LTG 3 Poster 13

Science Questions

Asthma does not impact all ages equally, it is seen as more common among children than adults. In the U.S. nearly 5 million asthma sufferers are under age 18, making it the most common chronic childhood disease. While 44% of all asthma hospitalizations are in children, 60% of the annual 4,000 deaths due to asthma occur in the senior citizens. In addition, early life factors are predictive for chronic asthma in adulthood. Therefore ORD research has centered on the key questions of:

1. What life stage confers increased risk of asthma from environmental factors?
2. What are the best factors of susceptibility related to differences in life stage?

Asthma outcomes vary depending on exposure during life stage. In utero diesel exposure increases cellular inflammatory in the offspring and alters levels of immune-regulatory molecules important in the development of allergic asthma. Maternal smoking will not only increase the asthma risk of children but also that of grandchildren nearly two-fold. Prenatal exposure to diesel PM and ETS can lead to increased respiratory symptoms and probable asthma by age 12 to 24 months.

Methylation and histone acetylation pattern changes induced by diesel suggests that epigenetic mechanisms may be responsible for it’s asthma trans-generational effects. Environmental exposures to barbiturate and porcine oil during the first year of life are associated with childhood asthma risk. Elevated Th2 status in one year old infants is associated with maternal agricultural work and may determine asthma and wheezing outcomes in their future. Life stage is a contributing factor that can lead to asthma development.

Research Goals

The goal of life stage research in asthma is to provide a fundamental understanding of the environmental factors that lead to increased risk to sensitive populations. Each ORD research has coordinated its research on asthma across the intramural, extramural programs and its cooperative agreements in focus on the research goals of this program:

1. Identifying critical windows of exposure that establish formation of asthma.
2. Understanding key environmental factors that drive life stage susceptibility to asthma.
3. Understanding the key pathways in asthma by which environmental factors differentially affect different life stages.

Epidemiology Studies

In New York, 305 pregnant women, believed to be at high risk for exposure to both PM and ETS were recruited. 48-h personal PM exposures were collected and their children monitored prospectively. By 24 months, difficulty breathing and probable asthma were reported more frequently among children exposed to prenatal PM and ETS postnatally.

The Detroit Children’s Health Study (see poster 3-11) has been used to recruit 220 non-atopic and atopic children aged 0-5 years into the Mechanistic Indicators of Childhood Asthma (MICA) study. By collecting clinical, genetic and biological samples we can identify and classify novel risk factors for asthma.

Identifying trans-generational asthma effects of in utero exposure to air pollutants

The CHAMACOS study in Monterey County, CA looked at the relationships between several environmental exposures during the first 12 months of life, and levels of Th1 and Th2 cytokines in 259 24-month-old children living in an agricultural community.

In vivo exposure of a pro-inflammatory cytokine (IL-1β) induced by DEP exposure involves chronic TLR9 modification and acetylation in bronchial epithelial cells.

The S. California Children’s health study (see poster 3-11) has studied lung function growth in a prospective study of children and soon deficits in growth of FEV1 in communities with high NO2 and associated pollutants. A nested case-control study using a questionnaire-based asthma design to select subjects has been used to identify early-life environmental factors for asthma.

Identifying early-life triggers of asthma

Life stages for ORD research is based on the categorization by the EPA Risk Assessment Forum and the Children’s Environmental Health Research highlight document with the addition of two groups: adolescents and older adults.

Future Directions

• Understanding how responses to microbes that may trigger asthma are modified by pollutants.

Results

Results used by California to support legislation limiting string of new schools in near proximity to major roadways.

Results used by New York City: to make that bus fleet must convert their fuel source to clean diesel.

Results used to support decision to install permanent EPA air monitors in Harlem.

Information used for criteria documents for ozone and particulate matter, the health assessment for diesel emissions, and the basis for the national ambient air quality standards for ozone.

Results will be used for hazard identification of compounds of diesel exhaust relevant if in auto alterations of immune function.

Information and results used to develop protocols for the National Children’s Study.

Methods/Approach

Central role of Life stage on induction/exacerbation of asthma.

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The CHAMACOS study in Monterey County, CA

Researchers Involved

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Results of the effect of exposure during gestation and during the first year of life to environmental factors such as allergens and air pollutants on the development of asthma.

Determining the critical gestational age in which exposure alters asthma risk.

Determining whether there are specific environmental factors specific to different subtypes of childhood asthma.

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Determining the effect of exposure during gestation and exposure to pollutants on the development of asthma.

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Determining whether there are environmental risk factors for exposure to both PAH and ETS were recruited. 48-h personal PM, and ETS exposures were collected and their children monitored prospectively. 24 months, difficulty breathing and probable asthma were reported more frequently among children exposed to prenatal PM and ETS postnatally.

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In vivo exposure of a pro-inflammatory cytokine (IL-1β) induced by DEP exposure involves chronic TLR9 modification and acetylation in bronchial epithelial cells.

Nadal cells from adolescents (15-19yrs) respond to diesel particles by making an increased inflammatory but decreased antioxidant response.

Sustainable Populations

Impact and Outcomes

• Omitting the effect of exposure during gestation and during the first year of life to environmental factors such as allergens and air pollutants on the development of asthma.

• Determining the critical gestational age in which exposure alters asthma risk.

• Identifying biomarkers in early life for evaluating interventions to reduce asthma.

• Determining whether there are specific environmental factors that increase the risk of developing new asthma in older adults.

• Determining whether there are environmental risk factors specific to different subtypes of childhood asthma.

• Understanding how responses to microbes that may trigger asthma are modified by pollutants.

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