Purpose of the Study. To determine if long-term exposure to air pollution adversely affects the growth of lung function during rapid lung development and if it has clinically significant adverse effects on final lung function attained during adolescence.

Study Population. Fourth-grade children (average age: 10 years) were enrolled and followed prospectively for 8 years.

Methods. Fourth-grade children (n = 1759) were recruited from elementary schools in 12 communities of southern California. Spirometric data were attained annually for 8 years. Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and midexpiratory flow rate were evaluated. The attrition rate of subjects was ~10% of subjects per year. Air pollution–monitoring stations were set up in the 12 study communities to measure exposures to ozone, acid vapor, nitrogen dioxide, particulate matter, elemental carbon, and organic carbon. Linear regression was used to examine the relationship of air pollution to the FEV1 and other spirometric measures.

Results. Over the 8-year period, deficits in the growth of FEV1 were associated with exposure to nitrogen dioxide (P = .005), acid vapor (P = .004), particulate matter with an aerodynamic diameter of <2.5 μm (PM2.5) (P = .04), and elemental carbon (P = .007) even after adjustment for several potential confounders and effect modifiers. Associations were also observed for other spirometric measures. Exposure to pollutants was associated with clinically and statistically significant deficits in the FEV1 attained at the age of 18 years. For example, the estimated proportion of 18-year-old subjects with a low FEV1 defined as a ratio of observed to expected FEV1 of <80% was 4.9 times as great at the highest level of exposure to PM2.5 as at the lowest level of exposure (7.9% vs 1.6%; P = .002). Exposure to ozone was not proven to be a contributor to lung-function deficit.

Conclusions. The results of this study indicate that current levels of air pollution in the communities evaluated have chronic, adverse effects on lung development in children from the age of 10 to 18 years. This long-term exposure leads to clinically significant deficits in attained FEV1 as children reach adulthood.

Reviewers’ Comments. This prospective study illustrates how chronic exposure to particular air pollutants negatively impacts the progression of lung function. From a public health perspective, it is important to consider and ameliorate environmental exposures that can have an adverse effect on final attainment of lung function.

Jennifer Maloney, MD
Scott H. Sicherer, MD
New York, NY

CHARACTERIZATION OF A COMMON SUSCEPTIBILITY LOCUS FOR ASTHMA-RELATED TRAITS


Purpose of the Study. Susceptibility to asthma is known to be hereditary, but the specific genes that determine the risk for asthma are not understood completely.

Study Population. The initial studies were conducted on a genetically isolated cohort in northern Finland, and the genetic associations were then confirmed in a separate cohort from Quebec. Finally, a mouse model of ovalbumin-induced lung inflammation was used to address mechanistic questions.

Methods and Results. Positional cloning was used to identify a 133-kilobase segment containing 2 genes that were associated with asthma risk and high IgE. One of these genes coded for a G protein-coupled receptor named G protein-coupled receptor for asthma susceptibility (GPRA); the B isofrom of this protein was found to be elevated in bronchial biopsies and smooth muscle from asthmatic individuals. Lung tissue of sensitized mice also expressed higher levels of GPRA mRNA.

Conclusions. Together, these data implicate GPRA in the pathogenesis of atopy and asthma and provide a novel therapeutic target for these disorders.


Purpose of the Study. To evaluate the role of vascular endothelial growth factor (VEGF) in T-helper type 2 (Th2) cell-mediated airway inflammation.

Study Population. Lung-targeted VEGF165 transgenic mice and wild-type mice.

Methods. Phenotypes of transgenic mice with elevated VEGF induced by doxycycline were studied and compared with wild-type mice. Airway histologic and physiologic assessments with special stains of microvasculatures, epithelium cells, inflammatory cells, smooth muscle cells, and dendritic cells (DCs) as well as allergen sensitization and methacholine tests were performed.

Results. Both Th2 and epithelial cells were primary sources of VEGF. Mice with overexpressed VEGF in the airways demonstrated increased neovascularization, mucous gland metaplasia, edema, collagen deposition, myocyte hyperplasia with enlarged smooth muscle bundles, inflammatory cells, activated DCs, airway hyperresponsiveness, interleukin 13 mRNA expression, Th2 responses, and allergen sensitization.

Conclusions. VEGF is a potent mediator of allergic airway inflammation by enhancing allergen sensitization, airway hyperresponsiveness, Th2 inflammation, and airway remodeling.

Reviewers’ Comments. Well-described airway pathology in asthma includes epithelial desquamation, goblet cell hyperplasia, collagen deposition below the basement membrane, smooth muscle hypertrophy/hyperplasia, and the growth and proliferation of new blood vessels. Al-
Characterization of a Common Susceptibility Locus for Asthma-Related Traits
James E. Gern
Pediatrics 2005;116;556
DOI: 10.1542/peds.2005-0698SS

Updated Information & Services
including high resolution figures, can be found at:
/content/116/Supplement_2/556.2.full.html

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Developmental/Behavioral Pediatrics
/cgi/collection/development:behavioral_issues_sub
Growth/Development Milestones
/cgi/collection/growth:development_milestones_sub
Pulmonology
/cgi/collection/pulmonology_sub
Respiratory Tract
/cgi/collection/respiratory_tract_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Characterization of a Common Susceptibility Locus for Asthma-Related Traits
James E. Gern
Pediatrics 2005;116;556
DOI: 10.1542/peds.2005-0698SS

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/116/Supplement_2/556.2.full.html