nonpharmacologic therapeutic strategy in obese adolescents who have asthma.

REVIEWER COMMENTS. Asthma and obesity are 2 chronic conditions that are becoming more prevalent in children today. Moreover, there is often a direct relationship between the 2 factors; increased BMI is associated with dose-dependent increases in asthma incidence and severity. The authors were able to limit their study subjects to obese prepubertal children, providing a clearer picture of how emphasizing a normocaloric diet not only can contribute to a decreased BMI but also to improved AR-QoL. Although many allergy practices have incorporated asthma educational strategies at diagnosis and follow-up, perhaps it is time to also include standardized nutritional recommendations. Encouraging our youngest patients with asthma to maintain a normal BMI may not only help reduce exacerbations and potential for steroid adverse effects but also contribute to optimal lung development during this critical growth period.

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β-2 Adrenergic Receptor Gene Methylation Is Associated With Decreased Asthma Severity in Inner-City Schoolchildren: Asthma and Rhinitis


PURPOSE OF THE STUDY. The B2-adrenergic receptor (B2AR) is the major target of β-agonist bronchodilators. The gene encoding the B2AR (ADRB2) has been mapped to chromosome 5q31-33, a region identified as a susceptibility locus for asthma or atopy. Epigenetic changes are heritable changes in gene expression, not encoded by DNA sequence changes (eg, methylation of cytosine-phosphate guanine [CpG] islands within regulatory regions of DNA). A variably methylated CpG island overlaps ADRB2. The purpose of this study was to determine the effects of methylation on asthma symptoms, morbidity, and lung function.

STUDY POPULATION. This study was nested within the SICAS (School Inner-City Asthma Study) and involved children who had a physician’s diagnosis of asthma within the past 12 months.

METHODS. DNA was extracted from saliva- and blood-derived samples. CpG sites were selected from the ADRB2 CpG island promoter region. DNA methylation assays were performed by staff blinded to the study. Methylation profiles for each locus represent a combination of saliva and blood sources. Caregivers completed questionnaires about asthma symptoms and rescue medication use within the past 4 weeks, as well as unscheduled health care visits and school absences related to asthma in the past 12 months. Subjects underwent prebronchodilator and postbronchodilator spirometry.

RESULTS. After adjusting for age, race, gender, preterm birth, family history of asthma, diagnosis of eczema, and sample source, percent methylation of the ADRB2 promoter showed a strong inverse association with dyspnea (odds ratio: 0.2; P = .002). There was no evidence of allele-specific differences in methylation.

CONCLUSIONS. This study is the first showing increased methylation at the ADRB2 gene being inversely associated with dyspnea, contributing to an improved asthma phenotype.

REVIEWER COMMENTS. Typically, DNA CpG hypermethylation leads to decreased expression of the gene product. Data are inconsistent regarding the relationship between B2AR density in the airways and severity of asthma. This study showed that methylation can play a role in asthma phenotypes. More polymorphisms will need to be studied before concluding that methylation is independent of genotype.

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Decreased Levels of Lipoxin A4 and Annexin A1 in Wheezy Infants


PURPOSE OF THE STUDY. The authors measured levels of lipoxin A4 (LXA4) and annexin A1 (ANXA1) in children with a history of infantile wheezing. Lipoxins and annexins are classes of mediators involved in the resolution of inflammation.

STUDY POPULATION. Fifty-nine children with a history of wheezing with no underlying disease and 28 healthy control subjects were recruited in this Turkish study. Ages ranged from 6 to 36 months, and all children had a history of ≥3 wheezing attacks with no previous corticosteroid treatment during the preceding month.

METHODS. Blood samples were taken to measure LXA4 and ANXA1 levels by using enzyme-linked immunosorbent assay. Total IgE levels and eosinophil counts were also measured.

RESULTS. No significant differences in total IgE levels were detected between children with wheezing and control children. LXA4 (66 ± 35 vs 120 ± 11 pg/mL; P < .05) and ANXA1 (14.45 ± 3.26 vs 16.40 ± 1.94 ng/mL; P < .05) levels were significantly lower in the wheezing group than in the control group. In the wheezing group, a significant correlation was found between the serum total IgE level and the percentage and absolute number of eosinophils (r = −0.223; P = .02). No correlation was
detected between groups when LXA4 levels, ANXA1 levels, total IgE levels, and the percentage and absolute number of eosinophils were calculated ($P > .05$).

CONCLUSIONS. Serum levels of LXA4 and ANXA1, which are known to be anti-inflammatory mediators, were low in wheezy infants. Decreased synthesis may be one of the reasons for airway inflammation in these infants.

REVIEWER COMMENTS. LXA4, which is expressed on leukocytes and airway epithelial cells, blocks both airway hyperresponsiveness and pulmonary inflammation. In adult studies, it has been shown that the level of LXA4 is low in patients with severe asthma. In experimental studies, ANXA1 is associated with the development of asthma. Smokers and those with inflammatory lung conditions such as cystic fibrosis and asthma have been found to have defective ANXA1 molecules. The authors in this study found that wheezing infants had lower LXA4 and ANXA1 levels, suggesting an increased susceptibility to recurring inflammatory changes in the airways. Following LXA4 and ANXA1 levels over time may be a way to help predict which children will develop childhood asthma and allow for earlier treatment interventions.

Applicability of the Global Lung Function Spirometry Equations in Contemporary Multiethnic Children

PURPOSE OF THE STUDY. In 2012, as a result of the Global Lung Function Initiative, the first global, all-age (3–95 years of age), multiethnic reference equations for spirometry (GLI-2012) were published. The authors of the present paper, as part of the Size and Lung Function in Children study, sought to investigate existing ethnic differences in lung function in a multiethnic population of children and to validate the GLI-2012 reference equations in this population.

STUDY POPULATION. Technically acceptable spirometric data were obtained from 1088 healthy children. The children were classified into 4 main ethnic groups: white, black, South Asian, and other/mixed.

METHODS. Spirometric data were expressed as percent predicted on the basis of the GLI-2012 equations for white subjects, adjusted for age, gender, and height and then on the basis of the ethnic-specific GLI-2012 equations.

RESULTS. When compared with white children, forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were significantly lower by a mean of $\sim$12% in black and Asian children and by 5% in other/mixed race children. FEV1 and FVC were reduced proportionally such that the FEV1/FVC ratio was unaffected. When data were expressed according to the GLI-2012 ethnic-specific reference equations, the mean FEV1 and FVC $z$ scores approximated 0, indicating that the GLI-2012 equations appropriately compensate for these ethnic differences.

CONCLUSIONS. The authors concluded that although there are significant ethnic differences in FEV1 and FVC in primary school-children, the magnitude of which is similar to that reported in older subjects, these differences can be minimized by using the GLI-2012 ethnic-specific reference equations.

REVIEWER COMMENTS. Just as in adults, there are marked ethnic differences in lung function in children, even after correcting for age, height, and gender, particularly for children of African or Asian descent. To generate accurate spirometric results, ethnic-specific reference equations should be used where available or corrections should be made to reference equations derived from white subjects by using appropriate percent reductions.

Validation of Parental Reports of Asthma Trajectory, Burden, and Risk by Using the Pediatric Asthma Control and Communication Instrument

PURPOSE OF THE STUDY. The goal of this study was to evaluate the utility of assessing direction, bother, and risk domains within the Pediatric Asthma Control and Communication Instrument (PACCI), a validated parent-completed questionnaire assessing 5 dimensions of asthma health, as part of guideline-recommended asthma care.

STUDY POPULATION. A convenience sample of 317 children diagnosed with asthma (mean age: 8.2 years; 58% boys; 44% African American) was recruited from 2 university-based asthma specialty care clinics.

METHODS. Cross-sectional data were collected on demographic characteristics, spirometric values (1 center), and results of several parent-completed questionnaires. The Pediatric Asthma Caregiver Quality of Life Questionnaire (PACQLQ) assessed asthma-specific quality of life, and asthma control was measured by using the validated PACCI control domain. Mean asthma PACCI control, PACQLQ, and lung function values were assessed across the domains of direction (asthma improving or worsening), bother, and risk by using analysis of variance. The PACCI was further analyzed for discriminative validity by using linear regression and $\chi^2$ analyses.

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