PURPOSE OF THE STUDY.


PURPOSE OF THE STUDY. Elevated fractional exhaled nitric oxide (FeNO) has been shown to be a sensitive biomarker for airway inflammation in children with asthma. This study examined whether a relationship could be demonstrated between genetic variants in nitric-oxide synthase and arginase genes and FeNO in asthma.

STUDY POPULATION. Subjects aged 5 to 7 years were recruited from 13 Southern California communities for a Children’s Health Study cohort established in 2003. Although FeNO data were available irrespective of race/ethnicity, genetic data were only available from Hispanic and non-Hispanic white children, and data from 2773 children were available for the combined analysis.

METHODS. FeNO measurements were made with breathsample collections that followed American Thoracic Society guidelines and took place in 2 consecutive school years. Variations in 5 genetic loci were characterized by tag single-nucleotide polymorphisms. Repeated-measures analysis of variance was used to evaluate the association between these genetic variants and FeNO.

RESULTS. Sequence variations in the NOS2A and ARG2 loci were globally associated with FeNO (P = .0002 and 0.001, respectively) but in opposite directions regarding FeNO levels. The ARG2 association was tagged by intronic variant rs3742879 with stronger association with lower FeNO levels. The directional change noted between FeNO levels and the above-mentioned genetic variants was more pronounced in the children with asthma than in those without asthma.

CONCLUSIONS. Variants in the nitric-oxide synthesis pathway genes jointly contribute to the differences in FeNO concentrations. Some of these genetic influences were stronger in children with asthma. Further studies are required to confirm these findings.

REVIEWER COMMENTS. Exhaled nitric oxide has become a more widely used tool in asthma patient care and clinical research settings. This report points out that there are genetic variants that could influence the interpretation of FeNO results. More studies are needed to determine the potential role of these genetic variants in the pathogenesis of asthma.
Genetic Variations in Nitric Oxide Synthase and Arginase Influence Exhaled Nitric Oxide Levels in Children

Stuart L. Abramson

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