**Exhaled Nitric Oxide is only an Asthma-relevant Biomarker among Children with Allergic Sensitization**

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**ABSTRACT** (250 words)

**Background**

Fraction of exhaled nitric oxide (FeNO) is used for diagnosing and monitoring asthma in children, but the influence of allergic sensitization is still poorly understood.

**Objective**

The aim of this study was to investigate how asthma and allergic sensitization influence FeNO levels during childhood.

**Methods**

We investigated the associations between asthma, aeroallergen sensitization, and FeNO levels measured from age 5 to 18 years in the COPSAC2000 birth cohort of 411 children using repeated measurement mixed models adjusted for gestational age, sex, concurrent airway infection, inhaled corticosteroids, and tobacco smoking. Replication was sought in the similarly designed COPSAC2010 cohort.

**Results**

Asthma and aeroallergen sensitization were both associated with higher FeNO levels from age 5 to 18 years: adjusted geometric mean ratio (aGMR), 1.22 (1.08-1.35), p<0.01, and 1.41 (1.21-1.65), p<0.001, respectively. However, asthma was associated with increased FeNO among children with aeroallergen sensitization: 1.44 (1.23-1.69), p<0.0001, whereas asthma was associated with decreased FeNO among non-sensitized children: 0.80 (0.65-0.99), p=0.05 (p-interaction<0.0001 for asthma x sensitization). Replication in the COPSAC2010 cohort showed similar results with p-interaction<0.01. Further, blood eosinophil count, total-IgE, bronchodilator response, and bronchial hyperreactivity were all associated with increased FeNO among children sensitized to aeroallergens, but not among non-sensitized children.

**Conclusions**

FeNO is elevated in children with asthma and correlated with asthma-associated traits dependent on aeroallergen sensitization.

**Clinical Implication**

FeNO is a biomarker of asthmatic airway inflammation in childhood, but only among children sensitized to aeroallergens. This should be acknowledged by physicians using FeNO for diagnosing and monitoring children with asthma.