Researchers identify early biomarker for future atopy in asymptomatic children

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The signs of atopy may be present long before symptoms begin, even in month-old babies, according to a new research study from Denmark. The study found that the level of urinary eosinophil protein-X (u-EPX), a marker of inflammatory cells, in newborn babies was linked to higher risk of allergic sensitization, nasal eosinophilia and eczema at six years.

The study appeared online in advance of the print publication of the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

"We asked whether the allergic disease process may be active prior to the development of symptoms, and if so, whether there are biomarkers that could be clinically useful in predicting the development of disease," said principle investigator Hans Bisgaard, MD, DMSci, professor of pediatrics at the University of Copenhagen. "We found that in babies born to asthmatic mothers, urine levels of eosinophil protein-X may predict the development of allergic symptoms."

The researchers measured the levels of u-EPX and several other markers of inflammation in 369 healthy month-old infants who were enrolled in the Copenhagen Prospective Study on Asthma in Childhood (COPSAC), a birth cohort study of symptom-free month-old children born to asthmatic mothers.

The children were evaluated for allergic sensitization to 16 common inhalant and food allergens at 6 months, 18 months, 4 years and 6 years.

Their blood eosinophil count was also taken at these intervals. Nasal eosinophilia was investigated by nasal scraping in the child's sixth year of life, and allergic rhinitis was diagnosed by age six based on interviews of parents and the child's history of symptoms. Asthma-like symptoms, and diagnoses of asthma and eczema were also noted.

In the first year of life, four percent of the children developed asthma-like symptoms and more than one-quarter (27 percent) were diagnosed with eczema. Another 17 percent went on to develop asthma-like symptoms and 15 percent developed eczema by age six.

When the researchers analyzed the data for associations between infant levels of u-EPX and future symptoms and diagnoses, they found that elevated u-EPX at one month was associated with 49 percent increase in risk of allergic sensitization, an association that was statistically significant for both food and aeroallergens. High u-EPX was also associated with a three-fold risk of developing nasal eosinophilia, indicating allergic inflammation of the upper airways. Finally, infants whose u-EPX was in the top quartile had a 40 percent greater risk for developing eczema by the age of six than those in the lower three quartiles.

"These data suggest that there is early life eosinophilic activation prior to symptom debut in children developing atopy-related conditions," said Dr. Bisgaard. "The mechanism behind the apparent pre-symptom eosinophilic activation in very young children is still unknown, but this study suggests that there is an ongoing pathogenesis in these children that begins well before symptom onset and includes the activation of eosinophil granulocytes."

Dr. Bisgaard noted that the current findings support similar findings of previous studies done in the same cohort. "These findings are in line with our previous studies, one where we saw increased concentration of

exhaled nitric oxide in the breath of these healthy babies preceding later development of lung symptoms, and one that showed an association between bacterial colonization in the airways and later risk of asthma. Together, these three studies support the concept that a disease process is present long before symptoms become present—'a patient is a patient before he is diagnosed as a patient'— and that the disease originates very early in life," he said.

"This knowledge may help us identify the highest risk groups of children from a very early age for targeted prevention as well as individualized intervention and treatment," he continued.
"This has redirected our research into what causes asthma, eczema and allergy, and we are now focusing on events in the first months of life or before birth."

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