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Early Antibiotic Use Linked to Asthma and Allergy at Age 6 Years

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January 11, 2011 — Early antibiotic use by age 6 months is linked to asthma and allergy at age 6 years, according to the results of a cohort study reported online December 29, 2010, in the *American Journal of Epidemiology*.

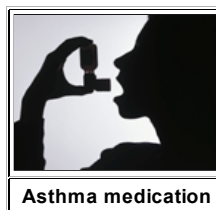
"Early antibiotic exposure, especially to broad-spectrum antibiotics, may suppress the developing immune system and produce a reduced anti-allergic response," said senior author Michael B. Bracken, professor of epidemiology at the Yale School of Public Health in New Haven, Connecticut, in a news release.

Although previous studies have shown an association of antibiotic use with an increased risk for childhood asthma, respiratory tract infections in young children may be confused with early symptoms of asthma. These studies may therefore have been confounded by "protopathic" bias if antibiotics are used to treat early symptoms of asthma.

"Addressing protopathic bias in studies on antibiotic use is challenging since children are commonly prescribed antibiotics for respiratory tract infections, which may be a sign of future asthma," Anita Kozyrskyj, PhD, associate professor and research chair of Maternal-Child Health and the Environment at Women and Children's Health Research Institute and Stollery Children's Hospital Foundation, University of Alberta in Edmonton, Canada, told *Medscape Medical News* when asked for independent comment.

"The authors of this study attempted to do this by excluding children with asthma diagnosed before 6 months, at the time that antibiotics were prescribed, and by conducting separate analyses in children without lower respiratory tract infections," Dr. Kozyrskyj said. "However, they did not conduct separate analyses on children receiving antibiotics to treat non-respiratory tract infections (both lower and upper) because they did not obtain information on the indication of the antibiotic. Even if they had, the study sample size would have been too small to conduct analyses on children receiving antibiotics for non-respiratory tract infections."

To evaluate the association between antibiotic use within the first 6 months of life and asthma and allergy at age 6 years, the investigators studied 1401 US children between 2003 and 2007. Children with early antibiotic exposure had an increased risk for asthma, with an adjusted odds ratio (OR) of 1.52 (95% confidence interval [CI], 1.07 - 2.16). In children in whom asthma was first diagnosed after age 3 years, the adjusted OR was 1.66 (95% CI, 0.99 - 2.79). In children who had no history of lower respiratory tract infection before age 1 year, the adjusted OR was 1.66 (95% CI, 1.12 - 3.46).



Asthma medication

Children with no family history of asthma had an even stronger association of early antibiotic use with subsequent development of asthma (adjusted OR, 1.89; 95% CI, 1.00 - 3.58; *P* for interaction = .03). Adjusted OR for a positive blood or skin test result for allergy was 1.59 (95% CI, 1.10 - 2.28).

"The main strengths of the study are comprehensiveness of data on pregnancy and postpartum events obtained from mothers shortly after delivery, attempts by the authors to address protopathic bias, and the conduct of separate analyses in children with and without parental asthma," Dr. Kozyrskyj said.

"As noted by the authors, the main study limitation is that both antibiotic use, and data on child asthma and skin prick testing were obtained from maternal report when children were 6 years old," Dr. Kozyrskyj explained. "Of greater concern is the completeness of recall of information on antibiotic use in their infants. Also, mothers were not asked for the specific name of the antibiotic to obtain data on whether the antibiotic was narrow or broad-spectrum. I would imagine that mothers would have had greater difficulty in remembering this level of detail."

Protopathic Bias Unlikely

On the basis of their findings, the study investigators concluded that early antibiotic use was associated with asthma

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and allergy at age 6 years and that protopathic bias was unlikely to account for the main findings.

"More judicious prescribing of antibiotics to infants, especially of broad-spectrum antibiotics, is required," Dr. Kozyrskyj said. "This is not a new recommendation. What is worrisome is the revision of clinical practice guidelines for the antibiotic treatment for ear infections in Canada and the US to include more broad-spectrum antibiotics. In Sweden and Norway, basic penicillin remains the antibiotic of choice."

Family History Confirmed Previous Findings

Dr. Kozyrskyj noted that the findings of a greater association between infant antibiotic use and asthma in children without a family history of asthma confirmed her published findings from a Canadian birth cohort of 14,000 children (*Chest*. 2007;131:1753-1759).

"It is well established that family history is a strong determinant of childhood asthma, and numerous genetic association studies have tried to confirm, without success, the specific genetic polymorphisms that are responsible," Dr. Kozyrskyj concluded. "Further prospective studies are required on larger populations of children which obtain data on antibiotic use from prescription databases and record indication of antibiotic use to better address protopathic bias. In addition, similar to the large, birth cohort study that my SyMBIOTA team of researchers is embarking on in Canada, further research on the effect of antibiotic use on infant gastrointestinal microbiota and immunity will confirm biologic mechanisms for how antibiotic use in infancy can lead to the development of asthma and allergic disease in children."

The National Institutes of Health and the Liaison Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology supported this study. The study authors and Dr. Kozyrskyj have disclosed no relevant financial relationships.

Am J Epidemiol. Published online December 29, 2010. [Abstract](#)

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