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Acetaminophen use in adolescents linked to doubled risk of asthma

New evidence linking the use of acetaminophen to development of asthma and eczema suggests that even monthly use of the drug in adolescents may more than double risk of asthma in adolescents compared to those who used none at all; yearly use was associated with a 50 percent increase in the risk of asthma.

 **AUDIO:** ATS Past President, John. E. Heffner, M.D., discusses research linking acetaminophen use to increased asthma and eczema risk in adolescents.

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The research results will be published online on the American Thoracic Society's Web site ahead of the print edition of the *American Journal of Respiratory and Critical Care Medicine*.

"This study has identified that the reported use of acetaminophen in 13- and 14 year old adolescent children was associated with an exposure-dependent increased risk of asthma symptoms," said study first author Richard Beasley, M.D., professor of medicine, at the Medical Research Institute of New Zealand on behalf of the International Study of Asthma and Allergies in Childhood (ISAAC).

As part of the ISAAC program, two written questionnaires and one video questionnaire were administered to more than 300,000 13- and 14 year old children in 113 centers throughout 50 countries, asking them to quantify their use of acetaminophen (none, "medium"— at least once in the last year, or "high"— at least once in the last month) and their asthma, eczema and allergy symptoms.

There was a significant association between acetaminophen use and risk of asthma and eczema. For medium users the risk of asthma 43 percent higher than non-users; high users had 2.51 times the risk of non-users. Similarly, the risk of rhinoconjunctivitis (allergic nasal congestion) was 38 percent higher for

medium users and 2.39 times as great for high users compared to non-users. For eczema, the relative risks were 31 percent and 99 percent respectively.

As this was a cross-sectional study, causality could not be determined. However, there is mounting evidence that suggests a causal link.

A longitudinal study on a small population in Ethiopia that examined the risk of asthma and allergies associated with acetaminophen use elucidated a temporal relationship between acetaminophen usage and the development of asthma and allergy symptoms, lending greater evidence to the possibility that acetaminophen usage may indeed cause the increased risk. This study will also be published online in advance of publication of the *American Journal of Respiratory and Critical Care Medicine*.

Moreover, in an earlier study from the United States, 13 and 14-year-old children with asthma were randomized to take either acetaminophen or ibuprofen after a febrile illness. For those whose illness was respiratory, there was an increased risk of a subsequent outpatient visit for asthma.

There are a number of biologically plausible explanations for how acetaminophen might increase risk of asthma and allergy. Acetaminophen may have a systemic inflammatory effect, possibly increasing oxygen stress resulting from the depletion of glutathione-dependent enzymes, which may in turn lead to enhanced TH2 allergic immune responses. Furthermore, acetaminophen may suppress the immune response to, and prolong the symptomatic illness from, rhinovirus infections, which are a common cause of severe asthma exacerbations in childhood.

Given the increased risk associated with acetaminophen usage, Dr. Beasley and colleagues calculated that the population attributable risks—the percentage of cases that might be avoided if the risk factor were to be eliminated—were indicative of a remarkable impact from acetaminophen usage.

"The overall population attributable risks for current symptoms of severe asthma were around 40 percent, suggesting that if the associations were causal, they would be of major public health significance," said Dr. Beasley. "Randomized controlled trials are now urgently required to investigate this relationship further and to guide the use of antipyretics, not only in children but in pregnancy and adult life."

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