Acetaminophen Use and Risk of Asthma, Rhinoconjunctivitis, and Eczema in Adolescents
International Study of Asthma and Allergies in Childhood Phase Three

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Rationale: There is epidemiological evidence that the use of acetaminophen may increase the risk of developing asthma. Objectives: To investigate the risk of asthma and other allergic disorders associated with the current use of acetaminophen in 13- to 14-year-old children in different populations worldwide. Methods: As part of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three, 13- to 14-year-old children completed written and video questionnaires obtaining data on current symptoms of asthma, rhinoconjunctivitis, and eczema, and a written environmental questionnaire obtaining data on putative risk factors, including acetaminophen use in the past 12 months. Measurements and Main Results: The primary outcome measure was the odds ratio (OR) of current asthma symptoms associated with acetaminophen use calculated by logistic regression. A total of 322,959 adolescent children from 113 centers in 50 countries participated. In the multivariate analyses the recent use of acetaminophen was associated with an exposure-dependent increased risk of current asthma symptoms (OR, 1.43 [95% confidence interval, 1.33–1.53]) and 2.51 [95% confidence interval, 2.33–2.70] for medium and high versus no use, respectively). Acetaminophen use was also associated with an exposure-dependent increased risk of current symptoms of rhinoconjunctivitis and eczema. Conclusions: Acetaminophen use may represent an important risk factor for the development and/or maintenance of asthma, rhinoconjunctivitis, and eczema in adolescent children.

Keywords: acetaminophen; ISAAC; asthma; rhinoconjunctivitis; eczema

Evidence is accumulating that the use of acetaminophen may increase the risk of developing asthma and that its widespread increasing use over the last 30 years may have contributed to the increasing prevalence of asthma in different countries worldwide (1, 2). The evidence is based primarily on epidemiological studies, which have reported that exposure to acetaminophen in the intrauterine environment (3–7), childhood (6, 8, 9), and adult life (10–13) is associated with an increased risk of asthma. The potential mechanisms for these effects of acetaminophen include oxidant-induced airways inflammation and enhanced Th2 responses.

What This Study Adds to the Field
Acetaminophen use may represent an important risk factor for the development and/or maintenance of asthma, rhinoconjunctivitis, and eczema in adolescents.

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* A complete list of members may be found before the beginning of the references.

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AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject
There is epidemiological evidence that exposure to acetaminophen in the intrauterine environment, early childhood, and adult life is associated with an increased risk of asthma. The potential mechanisms for these effects of acetaminophen include oxidant-induced airways inflammation and enhanced Th2 responses.

What This Study Adds to the Field
Acetaminophen use may represent an important risk factor for the development and/or maintenance of asthma, rhinoconjunctivitis, and eczema in adolescents.

METHODS

ISAAC Phase Three is a multicenter, multicountry, cross-sectional study of two age groups of schoolchildren (6- to 7-year-olds and 13- to 14-year-olds) chosen from a random sample of schools in defined geographical areas within each center (16, 17). The data for the 13- to 14-year-old children (referred to in this article as adolescents) are presented in this article. The study instruments were two written questionnaires and a video questionnaire that were completed by the adolescent. The first written questionnaire (prevalence) obtained data...
on demographic characteristics and on asthma, rhinoconjunctivitis, and eczema symptoms. The second written questionnaire (environmental) obtained data on a wide range of putative protective and risk factors for the development of asthma and allergic disorders. The written questionnaires were translated into the local language with back-translation into English (18). The video questionnaire showed different audiovisual scenes of clinical asthma. The complete written questionnaires and information concerning the video questionnaire can be found on the ISAAC Web site at http://isaac.auckland.ac.nz.

The question relating to acetaminophen use was:

“In the past 12 months, how often on average have you taken paracetamol (e.g., Panadol, Pamol)?” Never/At least once a year/At least once per month.

Adolescents in the 1+ per year (medium) and 1+ per month (high) categories were compared with those in the “never” category.

A participant was considered to have current asthma symptoms (current wheeze) if they provided a positive response to the written question “Have you had wheezing or whistling in the chest in the past 12 months?”

A participant was considered to have current symptoms of rhinoconjunctivitis if they provided positive responses to both these written questions:

“Have you ever had this itchy rash at any time in the past 12 months?” If yes, “This itchy rash at any time affected any of the following places—the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?” (These questions were preceded by the question “Have you ever had an itchy skin rash which was coming and going for at least 6 months?”).

Symptoms of severe asthma were defined by the responses to the following written questions:

1. “How many attacks of wheezing have you had in the past 12 months”? None/1 to 3/4 to 12/More than 12. Participants who reported four or more attacks were considered to have symptoms of severe asthma.
2. “In the past 12 months how often, on average, has your sleep been disturbed due to wheezing?” Never woken with wheezing/ Less than one night per week/One or more nights per week. A response of one or more nights per week was considered to indicate symptoms of severe asthma.
3. “In the past 12 months, has the wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?” Yes/No. A positive response was considered to indicate symptoms of severe asthma.

For the video questionnaire, participants viewed five scenes of clinical asthma and were asked to indicate whether they had experienced similar symptoms “ever,” and if yes, “in the past year.” A participant was considered to have current wheeze (video) if they provided a positive response “in the past year” to the first scene, showing a person wheezing at rest.

Adherence to the protocol was assessed by the ISAAC International Data Centre and centers with serious discrepancies were excluded.

Analysis

To be included in the analysis, centers were required to have studied at least 1,000 children and have a response rate of greater than 70%. Odds ratios (ORs) were calculated using generalized linear mixed models with a binomial distribution and logit link and with centers being modeled as a random effect. The analyses on all study participants were adjusted for sex, region of the world, language, and gross national income as previously described (9).

Multivariate analyses were conducted to investigate whether the association between symptoms and acetaminophen use were con-
in 322,959 adolescents from 113 centers in 50 countries contributing to the analyses presented. Following the exclusion of centers in which there was less than 70% data for any covariate, and of participants for whom there were missing data for any covariate, there were 180,887 adolescents from 77 centers in 36 countries included in the multivariate analyses.

The mean percentage of children exposed to acetaminophen at least once a month was 30%, with levels ranging from 2% in Taiwan to 68% in Nigeria (Figure 2A). The mean percentage of children exposed to acetaminophen at least once in the previous 12-month period was 73%, ranging from 41% in China to 92% in Panama.

**Asthma**

The reported use of acetaminophen in the past 12 months was associated with a significant exposure-dependent increased risk of current asthma symptoms (Table 1). In the adjusted analyses, the ORs for current asthma symptoms for medium (1+/y) and high (1+/mo) acetaminophen use compared with no use were 1.38 (95% confidence interval [CI], 1.31–1.46) and 2.36 (95% CI, 2.20–2.52), respectively.

**Figure 2.** Plot showing the odds ratios for the association between the reported use of acetaminophen in the past 12 months (at least once a month versus none) and (A) current wheeze, (B) current wheeze (video), and (C) severe asthma symptoms in 13- to 14-year-old children. Circles represent the odds ratios for each of the 77 centers in 36 countries; squares represents the global odds ratio. For every country, the percentage of children exposed to acetaminophen (at least once a month) is stated in brackets.
TABLE 1. THE ASSOCIATION BETWEEN ACETAMINOPHEN USE IN PAST 12 MONTHS AND ASTHMA SYMPTOMS

<table>
<thead>
<tr>
<th>Current wheeze</th>
<th>Odds Ratio (95% CI)</th>
<th>Adjusted† (Children with Complete Covariate Data)</th>
<th>Multivariate Analysis‡ (Children with Complete Covariate Data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current wheeze (video)</td>
<td>1.38 (1.31–1.46)</td>
<td>1.42 (1.34–1.52)</td>
<td>1.43 (1.33–1.53)</td>
</tr>
<tr>
<td>Severe asthma</td>
<td>1.25 (1.17–1.34)</td>
<td>1.29 (1.19–1.39)</td>
<td>1.33 (1.22–1.45)</td>
</tr>
<tr>
<td>Asthma ever</td>
<td>1.23 (1.17–1.28)</td>
<td>1.24 (1.18–1.31)</td>
<td>1.24 (1.17–1.31)</td>
</tr>
</tbody>
</table>

Definition of abbreviation: CI = confidence interval.

Current acetaminophen use: high = 1+ in past 12 months; medium = 1– in past 12 months; never = none in past 12 months.

† Adjusted for sex, region of the world, language, and gross national income.

‡ Adjusted for sex, region of the world, language, and gross national income. Analysis restricted to the centers included in the multivariate analyses.

A total of 180,887 children were included from 77 centers in 36 countries.

The reported use of acetaminophen was associated with a significantly increased risk of current asthma symptoms with acetaminophen use in 13- to 14-year-old adolescent children was associated with an exposure-dependent increased risk of asthma symptoms. The magnitude of the increased risks of current wheeze (video) and symptoms of severe asthma were similar to those for current wheeze. The population attributable risk for symptoms of severe asthma due to current acetaminophen use was 43%.

**Rhinocconjunctivitis and Eczema**

The reported use of acetaminophen in the past 12 months was associated with a significant dose-dependent increased risk of current symptoms of rhinocconjunctivitis and eczema (Table 3). The risk was observed in most regions of the world (Table 4, Figure 3). The population attributable risk for current symptoms of rhinocconjunctivitis and eczema associated with current acetaminophen use was 36% and 40%, respectively.

**DISCUSSION**

This study has identified that the reported use of acetaminophen in 13- to 14-year-old adolescent children was associated with an exposure-dependent increased risk of asthma symptoms. The association was present in all major regions of the world.
world and persisted in the multivariate analyses, which controlled for confounding variables. The magnitude of the association was substantial, with a 2.5-fold increased risk associated with frequent acetaminophen use at least once per month. Similar magnitudes of risk were observed with symptoms of severe asthma determined by written questionnaire and with current wheeze when assessed by video questionnaire, both measures of clinically significant asthma (20–23). The public health significance of the findings is suggested by the population attributable risk for symptoms of severe asthma due to acetaminophen of 43%. Significant associations were also observed between current acetaminophen use and the risk of the related conditions rhinoconjunctivitis and eczema.

These findings extend our previous observations from ISAAC Phase Three, that the use of acetaminophen in infancy and current use was associated with an increased risk of asthma symptoms in 6- to 7-year-old children. Although many of the methodological issues relating to the earlier study also apply to analyses in the 13- to 14-year-old age group, there are also some differences that are relevant to the interpretation of the study findings. First, the current study had greater power and worldwide representation, with around 320,000 adolescents from 113 centers in 50 countries compared with around 200,000 6- to 7-year-old children from 73 centers in 31 countries. Second, we used a video questionnaire in which the audiovisual presentation of clinical asthma in different situations was presented. Validation studies have shown that the video questionnaire has high sensitivity and specificity for identifying children with bronchial hyperresponsiveness, providing data relatively free from bias due to language and culture (20–22).

Confounding by indication represented the most important consideration in the interpretation of the primary 6- to 7-year-old results. Although many of the methodological issues relating to the earlier study also apply to analyses in the 13- to 14-year-old age group, there are also some differences that are relevant to the interpretation of the study findings. First, the current study had greater power and worldwide representation, with around 320,000 adolescents from 113 centers in 50 countries compared with around 200,000 6- to 7-year-old children from 73 centers in 31 countries. Second, we used a video questionnaire in which the audiovisual presentation of clinical asthma in different situations was presented. Validation studies have shown that the video questionnaire has high sensitivity and specificity for identifying children with bronchial hyperresponsiveness, providing data relatively free from bias due to language and culture (20–22).

Confounding by indication represented the most important consideration in the interpretation of the primary 6- to 7-year-old results.
TABLE 4. THE DOSE-DEPENDENT ASSOCIATION BETWEEN ACETAMINOPHEN USE IN THE PAST 12 MONTHS AND CURRENT SYMPTOMS OF RHINOCONJUNCTIVITIS AND ECZEMA IN DIFFERENT REGIONS OF THE WORLD

<table>
<thead>
<tr>
<th>Region</th>
<th>Current Rhinoconjunctivitis (No.)</th>
<th>Medium vs. Never</th>
<th>High vs. Never</th>
<th>Odds Ratio (95% CI)*</th>
<th>Current Eczema (No.)</th>
<th>Medium vs. Never</th>
<th>High vs. Never</th>
<th>Odds Ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>2,055</td>
<td>1.30 (1.01–1.67)</td>
<td>1.38 (1.07–1.78)</td>
<td>1.78</td>
<td>1.45 (1.14–1.85)</td>
<td>1.30 (1.01–1.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia-Pacific</td>
<td>3,096</td>
<td>1.40 (1.23–1.60)</td>
<td>1.95 (1.54–2.45)</td>
<td>881</td>
<td>1.29 (1.07–1.56)</td>
<td>1.57 (1.19–2.06)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>1,419</td>
<td>1.31 (0.92–1.85)</td>
<td>2.14 (1.55–2.97)</td>
<td>547</td>
<td>1.82 (1.09–3.02)</td>
<td>2.34 (1.44–3.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian subcontinent</td>
<td>1,987</td>
<td>1.40 (1.12–1.75)</td>
<td>2.29 (1.82–2.89)</td>
<td>793</td>
<td>1.05 (0.80–1.38)</td>
<td>1.78 (1.34–2.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>7,793</td>
<td>1.36 (1.19–1.56)</td>
<td>2.41 (2.11–2.76)</td>
<td>4,425</td>
<td>1.28 (1.07–1.53)</td>
<td>2.09 (1.75–2.49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>877</td>
<td>1.14 (0.84–1.54)</td>
<td>2.17 (1.61–2.92)</td>
<td>438</td>
<td>1.41 (0.90–2.21)</td>
<td>1.95 (1.23–3.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern and Eastern Europe</td>
<td>1,815</td>
<td>1.50 (1.27–1.76)</td>
<td>2.52 (2.08–3.06)</td>
<td>1,080</td>
<td>1.27 (1.04–1.55)</td>
<td>1.87 (1.47–2.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oceania</td>
<td>1,471</td>
<td>1.15 (0.84–1.59)</td>
<td>2.38 (1.75–3.24)</td>
<td>683</td>
<td>1.26 (0.74–2.16)</td>
<td>1.77 (1.05–3.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Europe</td>
<td>4,352</td>
<td>1.53 (1.29–1.80)</td>
<td>2.87 (2.42–3.40)</td>
<td>1,378</td>
<td>1.56 (1.25–1.93)</td>
<td>2.67 (2.14–3.33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Definition of abbreviation: CI = confidence interval.
Current acetaminophen use: high = 1+ times in past 12 months; medium = 1+ in past 12 months; never = none in past 12 months.

* Multivariate analysis included centers with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Covariates included maternal education, maternal smoking, current diet, siblings. Adjusted for sex, region of the world, language, and gross national income. A total of 180,887 children were included from 77 centers in 36 countries.

old ISAAC study findings of acetaminophen use in infancy (24–27). Indeed, since publication of the earlier ISAAC findings, there have been a number of reports from prospective cohort studies that the association between acetaminophen use in early life and the risk of asthma in later childhood could be explained by confounding, due to the close association between acetaminophen use and respiratory morbidity in early childhood (28–30). Although such confounding is less likely to be relevant to the current use of acetaminophen in adolescent children, it may still be present to some extent. Another possibility is that there could be confounding by reverse causation if adolescents with asthma were more likely to develop febrile illnesses or experience pain and as a result have greater acetaminophen use than nonaffected adolescents. There do not appear to be data to assess this proposition for the wide range of febrile illnesses affecting adolescents worldwide, although those with asthma may be more prone to migraine, for which acetaminophen may be prescribed (31). However, there is evidence that acetaminophen may cause greater nasal symptoms and signs and a reduced serum neutralizing antibody response when taken for rhinovirus infection (32). This observation is relevant both to our study findings and to consideration of the nature of the association between acetaminophen use for respiratory tract infections in infancy and development of asthma in later childhood.

Another consideration is that in many countries, acetaminophen is marketed as the preferred analgesic and antipyretic of choice in persons with asthma. Although this has the potential to result in preferential use of acetaminophen, the observation that the association was present in populations with widely differing lifestyles, standard of living, medical practice, and availability of information of over-the-counter products containing acetaminophen suggests that it may not have had a major contribution to the association observed.

It is likely that adolescents who frequently took acetaminophen were more likely to have received acetaminophen in earlier childhood and the risk of asthma may have been due to this earlier use. This cannot be assessed in our study as only information on current use of acetaminophen was obtained, although it is relevant that in the previous ISAAC analysis the risk of current use of acetaminophen in 6- to 7-year-old children existed independently of acetaminophen use in the first year of life, and vice versa.

Potential confounding by factors that influence the risk of developing childhood asthma and use of acetaminophen is inherent in cross-sectional population-based studies. To address this issue, the ORs were adjusted for center level factors, such as region of the world, language, and gross national income, and multivariate analyses were undertaken in which potential confounding factors at the individual level were controlled for. In the multivariate analyses, there was no reduction in the strength of the association between acetaminophen use and asthma, suggesting that there was no major confounding by these factors. This pattern differs from that observed in the analyses from the 6- to 7-year-old children, in which the strength of the association was reduced in multivariate analyses, suggesting that confounding was present.

With these considerations in mind we propose that the findings are consistent with cross-sectional and longitudinal epidemiological studies, which have reported that acetaminophen exposure in the intrauterine environment, throughout childhood, and in adult life is associated with an increased risk of asthma (1–16). The findings are also consistent with the one randomized controlled trial of acetaminophen use in children with asthma (14). In that study, children with asthma were randomly assigned to receive either acetaminophen or ibuprofen during a febrile illness. Children randomized to acetaminophen had an increased risk of an outpatient visit for asthma, an effect which was observed for the treatment of fever due to respiratory but not other infective causes. However, as the study did not include a placebo treatment it was not possible to determine whether the observed difference in morbidity was attributable to an increased risk with acetaminophen treatment or a decreased risk with ibuprofen.

Our findings complement the international ecological analyses based on data from countries that participated in ISAAC Phase One and the European Community Respiratory Health Survey in which a positive association between per capita consumption and acetaminophen and the prevalence of asthma in children and adults, respectively, was reported (33). An observation from these studies is that English-speaking countries, which have among the highest prevalence rates of asthma, also have among the highest acetaminophen use, suggesting that greater acetaminophen use may explain to some extent the higher prevalence of asthma in English-speaking countries.

Overall, the population attributable risks for current symptoms of asthma and symptoms of severe asthma were around 40%, suggesting that if the associations were causal, they would...
be of major public health significance. These compare with the population attributable risks of around 30% in the previous ISAAC study of 6- to 7-year-old children. Similar to the findings in 6- to 7-year-old children, we observed an association between current acetaminophen use and current rhinoconjunctivitis and eczema symptoms in 13- to 14-year-old adolescents, and that this association was independent of the presence of asthma. These observations suggest that acetaminophen may have systemic inflammatory effects, possibly through increasing oxygen stress resulting from depletion of glutathione-dependent enzymes, which may also lead to enhanced Th2 allergic immune responses (1, 2, 15). Both mechanisms could lead to greater allergic inflammation, resulting in the development or worsening of preexisting asthma, rhinoconjunctivitis, or eczema, depending on the organ systems affected. Furthermore, acetaminophen may suppress the immune response to, and prolong the symptomatic illness from, rhinovirus infections (32), which are a common cause of severe exacerbations of asthma in childhood (34) and adult life (35) and in infancy are associated with an increased risk of subsequent asthma (36). Similarly, a recent study of prophylactic acetaminophen given at the time of vaccination indicates that acetaminophen in routine antipyretic doses is capable of modulating immune responses (37).

In conclusion, the study findings add to the evidence that acetaminophen use in childhood may be an important risk factor for the development and/or maintenance of asthma. However, it is not possible in a study of this design to determine whether the positive association observed was causal. As a result, randomized controlled trials are now urgently required to investigate this relationship further and to guide the use of antipyretics not only in children but also in pregnancy and adult life.

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**References**


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29. Taiplainen T, Dunder T, Mötönen M, Pokka T, Uhari M. Adolescents with asthma or atopic eczema have more febrile days in early childhood: a possible explanation for the connection between paracetamol and asthma. *J Allergy Clin Immunol* 2010;125:751–752.


