Postnatal Maternal Smoking Increases the Prevalence of Asthma But Not of Bronchial Hyperresponsiveness or Atopy in Their Children*

Vidar Søysth, MD; Johny Kongerud, MD, PhD; and Jacob Boe, MD, PhD, FCCP

We have compared the prevalence of asthma, bronchial hyperresponsiveness (BHR), and atopy in relation to parental smoking in children aged 7 to 13 years. Information on the prevalence of asthma was obtained from a questionnaire, BHR was assessed by a methacholine challenge test, and atopy was defined as a positive response to a skin prick test. A complete history of the parents' smoking habits during their children's life, including prenatal smoking habits, was recorded. The prevalence of maternal smoking increased from 37.9% during pregnancy to 45.3% at the cross-sectional survey. None of the outcomes was significantly related to paternal smoking, whereas postnatal maternal smoking was positively associated with asthma (odds ratio [OR]=2.9; 95% confidence interval [CI], 1.3 to 6.1). A negative association between prenatal maternal smoking and atopy was found (OR=0.6; 95% CI, 0.3 to 0.9). We found no significant association between BHR and parental smoking. Our results indicate that postnatal maternal smoking increases the prevalence of asthma in the offspring without inducing BHR.

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Key words: asthma; bronchial provocation tests; cross-sectional study; epidemiology; pulmonary function; skin prick test; tobacco smoke

Several studies have indicated that parental smoking aggravates asthma1-2 and increases bronchial responsiveness3,4 in children with established disease. It is less clear whether exposure to environmental tobacco smoke (ETS) induces bronchial hyperresponsiveness (BHR) or enhances sensitization to allergens in children, thereby causing childhood asthma. Some studies have indicated a positive association between BHR and parental smoking5,6 whereas others have failed to link the prevalence of BHR to ETS exposure.7,8 A lack of association between a positive reaction to skin prick tests (SPT) and exposure to ETS has also been reported.9,10 Furthermore, if exposure to parental ETS induces BHR or increases sensitization to allergens in children, the relative importance of the children's age at the time of exposure remains to be investigated.11 Studies comparing the relative importance of prenatal and postnatal exposure are lacking in particular.11

We have conducted a cross-sectional study of respiratory disorders among children aged 7 to 13 years. A life-long history of exposure to ETS in each child was recorded, including the mothers' smoking habits during pregnancy. The objective of the study was to investigate the association between exposure to parental smoking and asthma, BHR, and the presence of a positive reaction to SPT in children.

Materials and Methods

Population and Questionnaires

The study was conducted in two valleys in western Norway. All the schoolchildren in the first, third, and fifth grades (ie, aged 7 to 13 years) were invited to participate in a cross-sectional study during the 1989 to 1992 winter seasons. One of the parents attended the examination with the child. All the children and their parents were informed about the aims of the study and the test procedures. The protocol was approved by the regional ethics committee. A total of 620 from 645 eligible pupils attended the clinical examination, ie, the overall response rate was 96.1%.

The parents received a respiratory questionnaire, including questions about the familial history of asthma or hay fever (FAM), bronchitis before 2 years of age (BTY), respiratory symptoms, and the parents' smoking habits at the time of the examination (Appendix). The questionnaire was completed by the parents prior to

*From the Health Department, Hydro Aluminium Árdal, Øvre Árdal, Norway, (Dr. Søysth), and the Department of Thoracic Medicine, Rikshospitalet, University of Oslo, (Drs. Søysth, Kongerud, and Boe).

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the day of the examination. Those children who gave an affirmative answer to the question: "Has the child ever had asthma?" were regarded as having asthma. A complete history of each parent's smoking habits from the child's birth to the date of the clinical examination was recorded prior to the SPT and the bronchial challenge. In addition, the accompanying parent was asked about the mother's smoking habits during pregnancy. The number of cigarettes smoked was not recorded.

**Skin Prick Test and Bronchial Challenge Test**

The SPT were performed on 556 of the attending 620 children who attended the examination using allergen-coated lancets (Phazet, Pharmacia, Uppsala, Sweden). All allergens were used: birch, timothy grass pollen, mugwort, *Dermatophagoides pteronyssinus*, Cladosporium, horse, cat dander, and dog dander. Histamine and saline solution were used as positive and negative controls. The volar aspect of the right forearm was used and the results were recorded after 15 min. The wheel size was recorded as the mean of the long axis and its perpendicular and was regarded as positive if it was ≥ 3 mm. Children who had a positive reaction to at least one of the SPTs were considered to have atopy regardless of the size of erythema.

Spirometry was performed using a pneumotachograph (Vitalograph, Birmingham, UK) that was calibrated daily to 5 L using a 1-L syringe. The test was accepted if the difference between the best and the second best test varied by less than 5% or 100 mL, whichever was larger. Methacholine challenge was performed using a shortened version of the protocol suggested by Cockcroft et al. and Kongerud and Søyseth. All the children whose baseline FEV1 was ≥70% of predicted were invited to perform the challenge test. If there was no history of asthmatic symptoms and the FEV1 was >80% of predicted, the inhalation started at 2.0 mg/mL. Otherwise the initial concentration was 0.125 mg/mL. The concentration was increased fourfold unless the FEV1 fell by more than 10% from one concentration to the next. Then the concentration of methacholine was doubled from one inhalation to the next. It was also doubled if the FEV1 had decreased to less than 90% of baseline. The test was continued until a decrease from baseline of 20% or the maximum concentration of 32.0 mg/mL was reached.

If the FEV1 was less than 70% of predicted, the child was asked to perform a reversibility test. After two inhalations of 0.1 mg of salbutamol (Ventoline), a second spirometry measurement was carried out 5 min later. The response to the methacholine challenge was expressed as PC20; *ie*, the concentration that caused a fall in FEV1 of 20% from baseline calculated by linear interpolation on the log-linear dose-response curve. A subject was regarded as having BHR if the PC20 was ≤8 mg/mL or the FEV1 increased by more than 10% at the reversibility test.

**Assessment of Exposure to ETS**

The following indices of exposure to ETS were used in the analyses: (1) Maternal: MPRE=1 if the mother smoked for more than 3 months during pregnancy, otherwise MPRE=0; MPOST=1 if the mother had ever smoked after her child's birth, otherwise MPOST=0; MPOST was divided into three subclasses: (1.1) M01=1 if the mother smoked during the child's first year of life, otherwise M01=0; (1.2) MCUR=1 if the mother was a current smoker at the time of the investigation, otherwise MCUR=0; (1.3) MHIGH=1 if the mother had smoked for more than 7 years, otherwise MHIGH=0. (2) Paternal smoking was classified accordingly as P01, PCUR, PHIGH, and FEVER if the father had ever smoked after the child's birth.

**Statistical Analyses**

Univariate associations were investigated using simple χ² statistics for categorical data and t tests for continuous data using a statistical package (SYSTAT). The following covariates were regarded as potential confounders to each of the three outcomes: age (at the time of the cross-sectional survey), gender, FAM, and BTY. The association among each of these covariates and asthma, atopy, and BHR was investigated separately and entered in the initial multivariate analyses if the univariate associations revealed a p value of 0.25 or less. Since the exposure indices were mutually correlated, their relationship to each of the outcomes was investigated using stratified analysis (Mantel-Haenszel test). The confidence intervals were estimated as suggested by Robins et al. The strategy of the bivariate analyses was as follows: (1) compare the effect of MPOST stratified for MPRE and vice versa. (2) Compare the effect of M01 and MCUR separately, stratified for MHIGH, and, conversely, the effect of MHIGH after the stratification of M01 and MCUR, respectively. Finally, (3) investigate the effect of exposure to paternal ETS as described in (2).

Finally, the effects of the significant indices of exposure on each of the outcome variables obtained from the bivariate analyses were investigated in multivariate analyses by logistic regression using a module (LOGIT) of our statistical package (SYSTAT). Backward model reduction was performed as suggested by Lemeshow and Hosmer. The effect of concurrent maternal and paternal smoking was investigated by including the product-term MPOST×FEVER.

**RESULTS**

Of the 620 subjects who participated in the cross-sectional examination, 573 (92.4%) performed spirometry and BHR was assessed in 529 (85.3%) using a methacholine challenge or reversibility test. The characteristics of the different subgroups are given in Table 1. The relationship among BHR, atopy, and age is shown in Figure 1. After stratification by age, the odds ratio (OR) of having BHR was 3.4 (95% confidence interval [CI], 2.0-6.0) in atopic children compared with nonatopic children.

The prevalence of parental smoking, including prenatal maternal smoking, is shown in Figure 2. The prevalence of maternal smoking increased from 37.9% during pregnancy to 45.3% at the time of the investigation, whereas the prevalence of paternal

| Table 1—Mean Age, Number of Female Subjects, and Asthmatics Among Those Children Who Completed the Questionnaire and Participated in the Bronchial Challenge and Skin Prick Tests |
|--------------------------|-----|-----|-----|-----|
| No.                      | 618 | 529 | 556 | 620 |
| Age, yr (SD)             | 9.3 (1.7) | 9.5 (1.7) | 9.4 (1.7) | 9.3 (1.7) |
| Female subjects          | 305 (49.4) | 255 (48.2) | 275 (49.5) | 306 (49.4) |
| Asthma                   | 51 (8.3) | 45 (8.5) | 45 (8.6) | *  |

*Two questionnaires missing.*
smoking decreased from 45.6% during the first year of life to 40.3% at the time of the cross-sectional survey. The prevalence of ever smoking during the children's life was 53.5% in both parental genders.

The crude prevalence of asthma, BHR, and atopy in relation to different categories of maternal and paternal smoking is shown in Tables 2 and 3, respectively. An increased prevalence of asthma was indicated in relation to postnatal maternal smoking, whereas the prevalence of BHR was approximately equal in the different categories of exposure to maternal tobacco smoke.

To investigate the effect of each of these indices of ETS, bivariate analyses were performed. After the stratification of prenatal maternal smoking, the OR of asthma was 2.6 (95% CI, 1.2 to 5.5) in those children whose mothers were postnatal smokers compared with never smokers. Nevertheless, none of the different postnatal indices M01, MCUR, or MHIGH was significantly associated with asthma. Similarly, BHR was not associated with any of the indices of maternal smoking.

Using the Mantel-Haenszel test, the OR of atopy was 0.5 (95% CI, 0.3 to 1.0) in those children who had mothers with a history of prenatal maternal smoking compared with no prenatal smoking after the stratification of postnatal maternal smoking. No significant relationship between atopy and postnatal maternal smoking was found after adjustment for prenatal smoking. The indices of paternal smoking were not associated with any of the outcome variables.

Prior to the multivariate analyses, the univariate associations among asthma, atopy, and the potential confounders were investigated separately. According to the selection criteria, the following covariates were included in the initial model-building process: (1) asthma: FAM, BTY, age, and gender (although the latter two covariates were not significant); and (2) atopy: age and gender. The results of these analyses are shown in Table 4. The OR of asthma was 2.8 (95% CI, 1.3 to 6.1) in children who had been exposed to postnatal maternal tobacco smoke compared with the children of never-smoking mothers. Similarly, the OR of having atopy was 0.5 (95% CI, 0.4 to 0.9) in children whose mothers smoked during pregnancy compared with children whose mothers were non-smokers during pregnancy. No significant effect modification by exposure to paternal ETS on maternal smoking was found.

The FEV1/FVC ratio was slightly lower (−0.7%) in children whose mothers were ever smokers compared with never-smoking mothers. This effect was even weaker regarding exposure to paternal smoking (−0.2%). None of these differences reached a significance level of 5% or less.
Table 2—Maternal Smoking Habits During Children’s Growth, Including Pregnancy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prenatal</th>
<th>Postnatal</th>
<th>First Year of Life</th>
<th>Current</th>
<th>Long (≥7 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes No</td>
<td>Yes No</td>
<td>Yes No</td>
<td>Yes No</td>
<td>Yes No</td>
</tr>
<tr>
<td>(%)</td>
<td>(9.4) (7.6)</td>
<td>(10.5) (5.6)</td>
<td>(9.2) (7.6)</td>
<td>(8.9)</td>
<td>(7.7)</td>
</tr>
<tr>
<td>BHR</td>
<td>26/197</td>
<td>44/279</td>
<td>35/250</td>
<td>30/223</td>
<td>49/306</td>
</tr>
<tr>
<td>(%)</td>
<td>(13.2) (16.0)</td>
<td>(15.8) (14.0)</td>
<td>(13.5) (16.0)</td>
<td>(15.9)</td>
<td>(13.9)</td>
</tr>
<tr>
<td>(%)</td>
<td>(15.9) (23.8)</td>
<td>(19.6) (22.8)</td>
<td>(16.7) (23.7)</td>
<td>(18.4)</td>
<td>(22.8)</td>
</tr>
</tbody>
</table>

Table 3—Paternal Smoking Habits During Children’s Growth

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ever Smoker</th>
<th>First Year of Life</th>
<th>Current</th>
<th>Long (≥7 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes No</td>
<td>Yes No</td>
<td>Yes No</td>
<td>Yes No</td>
</tr>
<tr>
<td>Asthma</td>
<td>32/330</td>
<td>25/281</td>
<td>17/250</td>
<td>19/251</td>
</tr>
<tr>
<td>(%)</td>
<td>(9.7) (6.6)</td>
<td>(8.9) (7.7)</td>
<td>(6.8)</td>
<td>(9.2)</td>
</tr>
<tr>
<td>BHR</td>
<td>47/290</td>
<td>40/248</td>
<td>39/281</td>
<td>31/216</td>
</tr>
<tr>
<td>(%)</td>
<td>(16.2) (13.4)</td>
<td>(13.9) (13.9)</td>
<td>(14.4)</td>
<td>(15.1)</td>
</tr>
<tr>
<td>Atopy</td>
<td>56/280</td>
<td>45/276</td>
<td>62/276</td>
<td>37/208</td>
</tr>
<tr>
<td>(%)</td>
<td>(20.0) (21.7)</td>
<td>(18.8) (19.8)</td>
<td>(17.8)</td>
<td>(23.0)</td>
</tr>
</tbody>
</table>

Discussion

In this study, we found that the prevalence of asthma was increased in children whose mothers had a history of postnatal smoking compared with children with never-smoking mothers. A significant decreased prevalence of atopy was associated with prenatal maternal smoking. The data also indicated that the prevalence of maternal smoking increased from pregnancy to the date of investigation contrary to the prevalence of smoking among Norwegian women in the age range 20 to 34 years in the same period. It therefore seems likely that mothers try to avoid cigarette smoking during pregnancy, whereas their smoking rates increase after the delivery of the child.

Although a significant association was found between postnatal maternal smoking and asthma, we were not able to demonstrate any association between asthma and maternal smoking and exposure to parental ETS during the first year of life in the offspring. This lack of association could be caused by misclassification of disease or exposure, or by selective avoidance of smoking during the first year of life. Firstly, selective underreporting of parental smoking among parents with asthmatic children cannot be excluded. Secondly, asthma during the first year of life may have been diagnosed as bronchitis. Thirdly, the parents may have forgotten whether their children had asthma during the first year of life. The first kind of misclassification is selective and should increase the number of cases among nonsmokers, whereas the second is probably random in terms of the exposure variable. Both these sorts of misclassification should bias the association toward the zero effect. The third explanation, however, may be differential, ie, the parents’ memory of their children’s health status may depend on whether the parents smoked. The direction of this bias is difficult to assess. The overall effect of a misclassification of previous exposure or disease may thus result in an overestimation of the association. The possibility of a dilution effect, however, is not unlikely.

Asthma was clearly positively associated with postnatal exposure to maternal smoking. We were not, however, able to demonstrate an excessive risk in any of the subindices of postnatal exposure such as first year of life or cumulative effect of exposure. Weitzman and coworkers found that the OR of developing asthma during the first year of life was 2.6 in children with smoking mothers as compared with the children of nonsmoking mothers. The similar associations between asthma and maternal smoking.

Table 4—The Odds Ratio (OR) of Asthma and Atopy in Children in Relation to Their Mothers’ Smoking Habits

<table>
<thead>
<tr>
<th>Variable</th>
<th>Asthma (OR 95 %CI)</th>
<th>Atopy (OR 95 %CI)</th>
</tr>
</thead>
</table>
| Maternal smoking  
Prenatal  | 0.6 (0.3-1.3)       | 0.6 (0.4-0.9)      |
| Postnatal | 2.8 (1.3-6.1)       | 1.1 (0.7-2.1)      |
| FAM       | 2.1 (1.1-4.2)       | 3.5 (1.9-6.4)      |
| BYT       | 3.5 (1.9-6.4)       | 3.5 (1.9-6.4)      |
| Age, yr   | 1.0 (0.9-1.2)       | 1.2 (1.0-1.4)      |
| Female/male | 1.2 (0.7-2.3)     | 0.6 (0.4-0.9)      |

*Denotes that the variable was not included in the model according to the selection criteria.
were estimated at 2.8 in children aged 3 to 4 years and 2.5 in children 7 to 9 years of age. In none of these studies were adjustments for previous exposure or cumulative exposure made. In our study, the OR of asthma was 2.8 in children whose mothers were ever smokers compared with never-smoking mothers; ie, in agreement with all the studies cited above. Hence, it seems likely that the increased risk of childhood asthma associated with maternal smoking is uniform across the age-exposure strata. Since postnatal maternal smoking was unrelated to BHR and atopy, we hypothesize that childhood asthma is provoked by exposure to maternal tobacco smoke rather than being induced by ETS.

Prenatal maternal smoking appeared to have a protective effect on the development of atopy in the offspring. A causal interpretation of this result is, however, unlikely. A comparison of cord serum revealed increased IgE and IgD levels in the offspring of mothers who were smokers compared with mothers who were nonsmokers during pregnancy,27 ie, apparently in conflict with our result. Although a parental history of asthma or hay fever was included as a covariate in the analyses, we believe that our result might be distorted due to the selective avoidance of tobacco smoking during pregnancy. The observation that the prevalence of maternal smoking increased from pregnancy to the time of the cross-sectional survey should support this explanation. Furthermore, the primary health care centers offer future mothers checkups every month during pregnancy. The attendance rates in these surveys are high and information about the effects of passive smoking on the fetus is emphasized at these follow-ups. It could be that those mothers with an increased risk of ETS-related disorders quit smoking. However, our results indicate that parental smoking does not increase allergy sensitization in children. This view is also supported by other studies.9,10

When it comes to BHR, the association with the different kinds of ETS exposure was close to the zero effect, thereby indicating that ETS does not induce structural changes in the bronchial mucosa.28 Other investigators have associated BHR in childhood with exposure to maternal smoking.5,6 These conflicting results could also be explained by the selection bias caused by selective avoidance of cigarette smoking among the parents.

In conclusion, our results indicate that postnatal maternal smoking increases the prevalence of asthma in the offspring without inducing BHR or enhancing sensitization to allergens. Thus, ETS exposure appears to provoke childhood asthma without inducing the disease.

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Appendix

Familial history of asthma or hay fever (FAM):
"Has anyone in the family had asthma or hay fever?" Bronchitis before 2 years of age (BTY).
"Has the child been treated by a doctor or hospitalized because of bronchitis before 2 years of age?"

Asthma:
"Has the child ever had asthma?"

Current parental smoking (MCUR, PCUR):
"Does the child’s mother smoke daily?"
"Does the child’s father smoke daily?"

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