

# Chronic Airway Diseases in Adult Life and Childhood Infections

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## Key Words

Childhood respiratory infection · Parents' smoking · Asthma · Bronchitis, chronic · Cough, chronic

## Abstract

**Background:** Respiratory disorders in childhood may predispose to pulmonary disease in late adult life. **Objectives:** The aim of this study was to evaluate the relationship between their effects in adult life and the characteristics of the respiratory system in childhood. **Methods:** A total of 10,224 parents and grandparents of students from 14 randomly selected primary schools in the city center were asked to answer questionnaires given to their children. 9,853 of 10,224 persons (the overall response rate was 96.3%) were eligible for analysis. In the questionnaire subjects were asked about respiratory system-related symptoms and characteristics. **Results:** Chronic cough [14.3 vs. 4.7%, OR 3.4 (2.6–4.4),  $p < 0.001$ ], chronic bronchitis [35.3 vs. 11.8%, OR 4.0 (3.4–4.8),  $p < 0.001$ ] and asthma [34.2 vs. 5.1%, OR 9.6 (8.0–11.5),  $p < 0.001$ ] in the childhood respiratory infection group were more common than in the control group. Childhood respiratory infections were associated with an increased risk of asthma (OR 5.6,  $p < 0.001$ ), chronic bronchitis (OR 2.3,  $p < 0.001$ ) and chronic cough (OR 1.5,  $p < 0.001$ ), after adjusting for possible confounding factors. In addition, the presence of dampness or visible mould, wall-to-wall carpets, pets at home and parents' smoking during childhood were associated with an increased risk of frequent childhood respiratory infections. **Conclusion:** These results indicated that frequent respiratory infections during childhood might play an im-

portant role in the occurrence of chronic airway diseases in adult life. The removing of risk factors for frequent childhood respiratory infections may reduce the subsequent risk of chronic airway disease in late adult life.

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## Introduction

The hypothesis that lower respiratory tract infections in early childhood lead to chronic pulmonary disease in late adult life has been difficult to test [1]. Relevant epidemiological studies, however, have provided conflicting results, and many are flawed by recall bias. A complete test of the hypothesis would require a follow-up of study subjects from birth to adulthood with monitoring of respiratory infections and pulmonary function [2]. It is suggested that these childhood respiratory illnesses make the adult lung unusually susceptible to the adverse effects of a variety of bronchial irritants and infectious agents [3]. Follow-up studies of infants and children show that certain pulmonary infections may cause persistent abnormalities of lung function. This suggests that infection of an organ system during a period of rapid growth may have permanent deleterious effects [4]. The majority of childhood respiratory infections are viral in origin, and great progress is being made in the understanding of their pathogenesis at the molecular level [5]. The impairment of pulmonary growth in utero and early childhood, as a consequence of undernutrition and lower respiratory tract infection, may play an important part in the devel-

**Table 1.** Demographic variables of the population studied regarding childhood infections

|                  | Frequent childhood respiratory infections |                          | p value |
|------------------|---|--------------------------|---------|
|                  | yes<br>1,099                              | no (control group) 8,872 |         |
| Age, years       | 43.9 ± 11.5                               | 45.6 ± 12.7              | 0.0001  |
| Female gender, % | 54.4                                      | 52.2                     | NS      |
| Education, %     |   |                          |         |
| None             | 15.7                                      | 11.3                     |         |
| Primary school   | 57.7                                      | 56.2                     |         |
| Secondary school | 18.2                                      | 23.6                     |         |
| High school      | 8.5                                       | 8.8                      |         |
| Monthly income   |   |                          |         |
| <USD 200, %      | 85.8                                      | 82.4                     | 0.005   |
| Smoking, %       | 38.3                                      | 35.6                     | 0.07    |
| PSC, %           | 54.2                                      | 44.3                     | 0.0001  |
| Dyspnea score    | 2.1 ± 1.8                                 | 1.1 ± 1.6                | 0.0001  |

PSC = Parents' smoking during childhood.

opment of chronic pulmonary disease in late adult life [6]. Respiratory disorders in children may predispose to later disease, and consequently it might be important to determine appropriate measures to prevent respiratory illness in childhood [7].

Thus, the aims of this study were to evaluate the effects of frequent childhood respiratory infections on the respiratory system in adult life and to explore predictors of frequent respiratory illness in childhood in a population-based study.

## Methods

### Study Population

The first epidemiological survey of the prevalence of respiratory symptoms and other diseases in Kirikkale, Turkey, was conducted in October 2004. A total of 10,224 parents and grandparents of students from 14 randomly selected primary schools in the city center were asked to answer questionnaires sent via their children and to return their responses again via their children. The parents were asked about respiratory system-related symptoms and characteristics in the questionnaire. All respondents signed an informed consent form, and the study was approved by the local ethics committee. A chronic nonproductive cough was defined as answering yes to the following question: 'Do you usually cough during the day or at night for a minimum of 3 months a year?' and additionally a negative answer to the question concerning phlegm ('Do you usually bring up any phlegm from your chest during the day or at night?'). Chronic bronchitis was defined as

cough and phlegm for a minimum of 3 months a year and for not less than 2 successive years [8].

For the purposes of this study, 'definite asthma' was defined as positive responses to all three of the following questions (ATS questions 20A, 20B, and 20C3): (1) 'Have you ever had asthma?', (2) 'Do you still have it?', and (3) 'Was it confirmed by a doctor?' [9].

Frequent respiratory infections during childhood were defined as a positive response to the question: 'Have you had frequent respiratory infections during childhood?' Subjects with a negative response were included in the control group.

Environmental exposure to parental tobacco smoking was defined as a positive response to the question: 'Did your father or mother ever smoke regularly during your childhood?'

The questions on mould or dampness were as follows: (1) 'Have you had mould growth on the surfaces in any of your dwellings during childhood?' (2) 'Have you had damp stains, for example, on the walls or on the ceilings of any of your dwellings during childhood?' (3) 'Has there been a leak or water damage in any of your dwellings during childhood?'

For the definition of visible mould or dampness at home a positive response to three questions was necessary [10]. The presence of wall-to-wall carpets at home was defined as a positive response to the question: 'Did you have wall-to-wall carpets in your home during your childhood?' The presence of pets at home was defined as a positive response to the question: 'Did you have pets in your home during your childhood?'

All questions had to be answered with either 'yes' or 'no', not with 'as far as I know'.

### Statistical Analyses

Analyses were performed separately for the three case groups that did not overlap: asthma, chronic bronchitis and chronic cough. For the purpose of subsequent analyses, persons with asthma (yes/no), chronic cough (yes/no), or chronic bronchitis (yes/no) were put into separate groups. The  $\chi^2$  test (or, when appropriate, Fisher's exact test) was used for testing differences in the prevalence of symptoms between groups. Prevalence odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated with the Mantel-Haenszel method. For comparisons of continuous variables a t test was performed. Smokers included ex-smokers and current smokers. Logistic regression was used to calculate OR and 95% CI for the association between asthma, chronic bronchitis and chronic cough with exposure to smoking during childhood, frequent respiratory infections during childhood, gender and age (0 = <60 year; 1 = ≥60 year). Independent variables were entered into the logistic model using a forward procedure. Data were expressed as mean ± SD. All analyses were performed using the SPSS for Windows (version 10.01; SPSS, Chicago, Ill., USA).  $p < 0.05$  was assumed to be statistically significant.

## Results

9,853 of 10,224 persons (the overall response rate was 96.3%) were eligible for analysis. The demographic characteristics of the population studied regarding childhood infections can be seen in table 1. In adult life, subjects in

**Table 2.** Risk factors for asthma, chronic bronchitis and chronic cough in adult life after adjusting for gender, age, smoking, income and education in logistic procedures

|                               | Asthma |         |         | Chronic bronchitis |         |         | Chronic cough |         |         |
|-------------------------------|--------|---------|---------|--------------------|---------|---------|---------------|---------|---------|
|                               | OR     | 95% CI  | p value | OR                 | 95% CI  | p value | OR            | 95% CI  | p value |
| Gender                        | 0.5    | 0.4–0.6 | 0.00001 |                    |         | 0.1     |               |         | 0.1     |
| Increased age                 | 1.9    | 1.5–2.4 | 0.00001 |                    |         | 0.05    | 1.9           | 1.5–2.5 | 0.00001 |
| Low income                    |        |         | 0.1     | 1.4                | 1.2–1.8 | 0.0001  | 1.5           | 1.0–2.2 | 0.01    |
| Education                     | 0.8    | 0.7–0.8 | 0.00001 | 0.8                | 0.7–0.8 | 0.00001 | 0.7           | 0.6–0.7 | 0.00001 |
| Smoking                       | 1.2    | 1.0–1.5 | 0.03    | 1.8                | 1.6–2.1 | 0.00001 |               |         | 0.6     |
| FCRI                          | 5.6    | 4.7–6.8 | 0.00001 | 2.4                | 2.0–2.8 | 0.00001 | 1.6           | 1.2–2.1 | 0.0004  |
| Dampness or visible mould     | 1.5    | 1.2–2.0 | 0.0001  | 1.5                | 1.3–1.8 | 0.00001 |               |         | 0.08    |
| Wall-to-wall carpets          | 1.9    | 1.3–2.6 | 0.0001  |                    |         | 0.3     |               |         | 0.05    |
| PSC                           |        |         | 0.1     | 1.3                | 1.1–1.4 | 0.00001 | 1.4           | 1.1–1.7 | 0.0004  |
| Pets at home during childhood | 1.4    | 1.1–1.7 | 0.003   |                    |         | 0.8     |               |         | 0.3     |

FCRI = Frequent childhood respiratory infections; PSC = parents' smoking during childhood.

the childhood respiratory infection group had a higher dyspnea score than those without respiratory infection during childhood.

Chronic cough [14.3 vs. 4.7%, OR 3.4 (2.6–4.4),  $p = 0.0001$ ], chronic bronchitis [35.3 vs. 11.8%, OR 4.0 (3.4–4.8),  $p = 0.0001$ ] and asthma [34.2 vs. 5.1%, OR 9.6 (8.0–11.5),  $p = 0.0001$ ] were more common in the childhood respiratory infection group than in the control group.

The logistic regression analysis showed that childhood respiratory infections were independent risk factors for asthma, chronic bronchitis and chronic cough, after adjusting for age, gender, income, education, and smoking (table 2). Frequent childhood respiratory infections were associated with an approximately 2-fold increased risk of asthma relative to chronic bronchitis.

The prevalence of dampness or visible mould, wall-to-wall carpets and pets at home and parents' smoking during childhood was significantly higher in those with a positive history of frequent respiratory infections during childhood than in those with a negative one (table 3). Multiple logistic regression (forward model) indicated that the presence of dampness or visible mould, wall-to-wall carpets and pets at home and parents' smoking during childhood are risk factors for frequent childhood respiratory infections (table 4). In addition, the strength of the association between frequent childhood respiratory infections and wall-to-wall carpets was higher than that of the presence of dampness or visible mould and pets at home and parents' smoking during childhood.

**Table 3.** Characteristics of frequent childhood respiratory infections in population

|                               | Frequent childhood respiratory infections |      |     |         |         |
|-------------------------------|---|------|-----|---------|---------|
|                               | yes                                       | no   | OR  | 95% CI  | p value |
| Dampness or visible mould     | 17.0                                      | 8.6  | 2.1 | 1.8–2.6 | 0.0001  |
| Wall-to-wall carpets          | 7.8                                       | 3.2  | 2.5 | 1.9–3.2 | 0.0001  |
| PSC                           | 54.2                                      | 44.3 | 1.4 | 1.3–1.6 | 0.0001  |
| Pets at home during childhood | 15.5                                      | 10.7 | 1.5 | 1.2–1.8 | 0.0001  |

PSC = Parents' smoking during childhood.

**Table 4.** Risk factors for frequent childhood respiratory infections after adjusting for gender in forward logistic procedures

|  | Frequent childhood respiratory infections |         |         |
|--|---|---------|---------|
|  | OR  | 95% CI  | p value |
| Gender                                     |   |         | 0.1     |
| Parents' smoking during childhood          | 1.4                                       | 1.2–1.6 | 0.00001 |
| Pets during childhood                      | 1.3                                       | 1.1–1.6 | 0.0008  |
| Dampness or visible mould during childhood | 1.9                                       | 1.6–2.3 | 0.00001 |
| Wall-to-wall carpets during childhood      | 2.1                                       | 1.6–2.8 | 0.00001 |

243 subjects were excluded because data were not available.

## Discussion

These results, from a population sample, indicated that frequent respiratory infections during childhood might play an important role in the occurrence of chronic airway diseases in adult life. However, the association between childhood respiratory infections and asthma was stronger than that of chronic bronchitis and chronic cough, after adjusting for age, gender, low income, education and smoking, when analyses were separately performed in a multivariate model (OR = 5.6 vs. 2.3 and 1.5). Accordingly, it may be suggested that respiratory infections in early life may increase the subsequent risk of asthma more than that of chronic cough and chronic bronchitis.

A study of a total of 8,008 randomly selected inhabitants aged 15–69 years showed that childhood exposure to environmental tobacco smoke is associated with an increased prevalence of asthma among adult never-smokers, especially in nonatopic subjects [11].

In another study including 15,901 subjects aged 20–44 years from random population samples in 37 areas participating in the European Community Respiratory Health Survey, both intrauterine and environmental exposure to parental tobacco smoking was related to more respiratory symptoms and poorer lung function in adulthood [12]. However, childhood respiratory infections have not been evaluated in these studies. In a study conducted in 3,700 elderly participants with a mean age of 76 years, multiple logistic regression yielded the following predictors for chronic bronchitis: male gender [OR = 1.1 (0.9–1.3)], previous smoking [OR = 1.7 (1.2–2.2)], present smoking [OR = 2.1 (2.1–3.8)], previous exposure to dust and fumes [OR = 2.2 (1.7–2.7)], chest infections in childhood [OR = 2.1 (1.6–2.9)], more than 6 chest infections in the previous 10 years [OR = 6.2 (4.1–9.2)] and alcohol consumption of more than 3 drinks a day [OR = 1.8 (1.3–2.3)] [13]. Another study also indicated that the prevalence of chronic bronchitis in the infection group in adult life (12.2 vs. 2.2%) is significantly higher than in the group without respiratory infection during childhood. Further analysis showed that infection and smoking had synergic effects on the occurrence of chronic bronchitis [14]. In addition, Barker and Osmond [15] observed that infection in early childhood had a greater influence than cigarette smoking in determining the geographical distribution of chronic bronchitis in adult life. In part, the present results are in agreement with results of the above studies. In contrast, a study of a random population sample of 1,104 subjects (aged 20–40 years), participating in the European Respi-

ratory Health Survey in Italy, indicated that exposure to serious childhood respiratory infections is a risk factor for asthma in the past (i.e., asthma in childhood and adolescence) but not for adult asthma or for the development of bronchial impairment in adult life [16].

Furthermore, the present study indicated that in adult life the subjects in the childhood respiratory infection group had a higher dyspnea score than those without respiratory infections during childhood. Accordingly, it may be considered that a group with frequent respiratory infections during childhood may have lower lung function. Similarly, other studies showed that lower respiratory tract infections in early childhood are associated with lower levels of lung function in late adult life [1, 3, 6, 17–23].

Lastly, the presence of dampness or visible mould, wall-to-wall carpets and pets in the household and exposure to smoking during childhood are risk factors for frequent childhood respiratory infections in logistic procedures. Previous studies suggested that exposure to smoking during childhood was associated with respiratory disease in adulthood [24, 25]. However, the present study suggests that exposure to environmental tobacco smoke in childhood was a risk factor for frequent childhood respiratory infections. It may be suggested that chronic airway disease in the late adult life may occur as a result of the parents smoking during childhood, resulting in frequent childhood respiratory infections, independent of its direct effects. A population-based case-referent study indicated that self-reported domestic exposure to moulds (OR 2.2) or environmental tobacco smoke (OR 2.4) could be associated with adult-onset asthma [25].

As in other epidemiological studies there are potential limitations in this study. Our study was also limited by relying on self-reports of the diagnosis of asthma and other diseases, and no quantification of pulmonary function was available. People are more likely to report respiratory symptoms if they have an abnormal psychological condition such as anxiety or depression [26]. The present study has suggested that respiratory infection during childhood is associated with respiratory disease in adulthood, but the link is unclear because of the retrospective evaluation of childhood infection and risk factors. In addition, a distinction between cough, bronchitis, asthma and COPD is very difficult in population surveys [27, 28]. The potential limitations of the present study should be well known and evaluated with caution. However, according to our knowledge, this is the first study comparing the effects of childhood risk factors for three chronic airway diseases.

In conclusion, our findings provide additional evidence for a causal relation between frequent childhood respiratory infections and adult respiratory disease. The removing of risk factors for frequent childhood respira-

tory infections may partially reduce the subsequent risk of chronic airway disease in late adult life. These findings should be supported by further prospective longitudinal studies.

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