



# Irreversible airway obstruction in adulthood after bronchiolitis in infancy: Evidence from a 30-year follow-up study



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## KEYWORDS

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## Summary

**Aim:** Lower respiratory infections in infancy may be associated with lung function deficits in adulthood. Our aim was to evaluate lung function, with a special focus on irreversible airway obstruction, thirty years after bronchiolitis or pneumonia in infancy.

**Methods:** In 1981–1982, 83 children under two years of age were hospitalized for bronchiolitis and 44 for pneumonia at Kuopio University Hospital, Finland. In 2010, 47 bronchiolitis patients, 22 pneumonia patients and 138 controls attended the study, including spirometry before (pre-BD) and after bronchodilatation (post-BD). The measured indices were forced vital capacity (FVC) and forced expiratory volume in one second (FEV<sub>1</sub>), that were presented as % of predicted value (FVC% and FEV<sub>1</sub>%). FEV<sub>1</sub>/FVC was presented as both absolute FVC/FEV<sub>1</sub>-ratio and % of predicted (FEV<sub>1</sub>/FVC%). Irreversible airway obstruction was defined as post-BD FEV<sub>1</sub>/FVC% below 88% of predicted (FEV<sub>1</sub>/FVC% <88%) according to Finnish reference values or FEV<sub>1</sub>/FVC-ratio below fifth percentile (FEV<sub>1</sub>/FVC <5th percentile), according to Global Lung Function Initiative reference values.

**Results:** All lung function indices were lower in former bronchiolitis patients and pre- and post-BD FEV<sub>1</sub>% in pneumonia patients, compared to controls. 21% of bronchiolitis (OR, 95%CI; 5.59, 1.72–18.21) and 9% of pneumonia patients (2.24, 0.34–13.56) had FEV<sub>1</sub>/FVC% <88% compared to controls (4%). Likewise 7 (15%) of bronchiolitis (7.07, 1.33–37.22) and 1 (5%) of pneumonia patients (1.73, 0.12–24.77) had FEV<sub>1</sub>/FVC <5th percentile compared to controls 2 (1%).

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*Conclusion:* Evidence of reduced lung function was present 30 years after hospitalization for bronchiolitis or pneumonia in infancy. Irreversible airway obstruction after severe bronchiolitis in infancy suggests permanent, structural alterations in airways.

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## Introduction

The association between lower respiratory infections (LRI) like bronchiolitis and pneumonia in infancy and increased risk of lung function disorders in childhood has been demonstrated in several studies [1,2], including a recent systematic review and meta-analysis on long-term sequelae of early childhood pneumonia [3]. In addition, LRI's in infancy have been associated with subsequent lung function disorders even in adulthood [4–8]. In the Swedish post-bronchiolitis follow-up study, airway obstruction was found in both pre- and post-bronchodilator measurements at the age of 17–18 years indicating that the obstruction was irreversible [7].

In birth cohort studies, reduced lung function has been present in infancy before any respiratory infection, and evidently reduced lung function predisposes an infant to both early childhood LRI's and subsequent wheezing [9–12]. Moreover, subjects with reduced lung function in early life were at an increased risk for permanent bronchial obstruction at the age of 22 years, even in the absence of any persistent symptoms [13].

We have followed a group of patients hospitalized for bronchiolitis or pneumonia in early childhood in 1981–1982, and found an increased risk of both asthma and lung function disorders up to the age of 18–20 years [8]. In 2010, when the study subjects were 28–31 years old, hospitalization for bronchiolitis in infancy was associated with an increased risk for asthma and hospitalization for both bronchiolitis and pneumonia with an impaired quality of life in adulthood [14].

In the present study, we evaluated lung function by using flow volume spirometry (FVS), including both pre-bronchodilator (pre-BD) and post-bronchodilator (post-BD) measurements in these former infantile bronchiolitis and pneumonia patients, and in matched population controls, at the age of 28–31 years. We hypothesized that permanently reduced lung function, and irreversible obstruction in particular, may be present in young adults after severe LRI in infancy. If the hypothesis is true, LRI in early childhood may predispose infants even to chronic obstructive pulmonary disease (COPD) in later adulthood. The aim of the study was to evaluate if reduced lung function and irreversible bronchial obstruction are present at the age of 28–31 years after bronchiolitis or pneumonia in infancy.

## Material and methods

### Study subjects

In 1981–1982, altogether 127 patients were hospitalized for bronchiolitis ( $N = 83$ ) or pneumonia ( $N = 44$ ) at less than

two years of age in the Department of Pediatrics, Kuopio University Hospital, Finland. Data on wheezing history, presence of asthma, and risk factors for asthma were collected at repeated control visits until the age of 18–20 years [8,15]. As published recently [14], an invitation to the study and a written questionnaire were sent to 122 study subjects with current addresses available. The questionnaire included inquiries about previous asthma diagnoses and current respiratory symptoms, like wheezing episodes, and medication used for asthma during the preceding 12 months [14].

In 2010, 48 (57.8%) former bronchiolitis and 22 (50.0%) former pneumonia patients attended the clinical study, which consisted of a doctoral interview and examination, FVS including both pre-BD and post-BD measurements, and monitoring two-week home peak expiratory flow (PEF). An invitation to the study was also sent to 488 population-based controls born in the area of Kuopio University Hospital and they were matched for sex and age (birth month). Four control subjects, who answered the questionnaire and had been hospitalized for lower respiratory tract infection at less than 24 months of age, were excluded. Altogether 138 (28.3%) of the invited controls attended the clinical study [14].

Acceptable FVS was obtained from all but one of the study subjects and from all controls. Thus, 47 former bronchiolitis patients, 22 former pneumonia patients, and 138 controls formed the material of the present lung function study.

### Presence of asthma and smoking

There were significant differences in current asthma and current smoking between the two study groups (bronchiolitis in infancy, pneumonia in infancy) and population controls [14]. Seventeen (36.2%) former bronchiolitis patients, 5 (22.7%) former pneumonia patients and 20 (14.5%) controls had asthma [14]. Asthma diagnosis was settled based on previous doctor-diagnosed asthma, usage of asthma medication, asthma-presumptive symptoms, and a pathological result in the home PEF monitoring [14]. Fourteen (29.8%) former bronchiolitis patients, 10 (45.5%) former pneumonia patients and 17 (12.3%) controls were current daily smokers (one cigarette or more smoked daily during the preceding 12 months) [14]. The median of the smoked pack-years was 0.1 (Range 0.0–25.0,  $p = 0.027$ ) in the bronchiolitis group and 0.5 (0.0–22.5, 0.064) in the pneumonia group, compared to 0.0 (0.0–25.0) in controls.

### Lung function data

Baseline lung function was measured with a Medikro SpiroStar USB spirometer (Medikro, Kuopio, Finland) using

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