

EFFECT OF PNEUMONIA AND WHOOPING COUGH IN CHILDHOOD
ON ADULT LUNG FUNCTION

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ABSTRACT

Background Previous studies have suggested that respiratory infection during childhood is associated with respiratory disease in adulthood, but the link is unclear because of retrospective ascertainment of childhood infection, selection bias, and confounding factors.

Methods We studied the effects of childhood pneumonia and whooping cough in 1392 British adults followed from their births in 1958. Of these, 193 had a history of pneumonia and 215 a history of whooping cough by the age of seven years. When the subjects were 34 or 35 years old, their forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were measured before and after they inhaled albuterol.

Results A history of pneumonia was associated with deficits (± 95 percent confidence limits) in both FEV₁ (102 ± 73 ml, $P=0.006$) and FVC (173 ± 70 ml, $P=0.001$) when the analysis was adjusted for sex, height, and smoking, with no change in the ratio of FEV₁ to FVC. These deficits persisted after inhalation of albuterol. In subjects with no history of wheezing, the deficit in FEV₁ was 155 ± 122 ml ($P=0.01$), in those with past wheezing it was 41 ± 128 ml ($P=0.53$), and in those with current wheezing it was 119 ± 133 ml ($P=0.08$). The effect was no greater for the subjects who had pneumonia at less than two years of age than for those who had it between the ages of two and seven years and was not diminished after control for multiple confounding factors. The deficits associated with whooping cough were smaller (FEV₁, 41 ± 70 ml; $P=0.25$; FVC, 81 ± 76 ml; $P=0.04$).

Conclusions Childhood pneumonia is associated with reduced ventilatory function in adults. This reduction is independent of a history of wheezing and is not explained by other confounding factors. (N Engl J Med 1998;338:581-7.)

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MANY studies have suggested an association between respiratory infection during childhood and the development of chronic obstructive pulmonary disease in adulthood.¹⁻³ The nature of such a link remains unclear, however, because of retrospective ascertainment, selection bias, and confounding factors. Only three population studies have reported independent information on both lower respiratory tract infection in childhood and lung function in adults.⁴⁻⁶ These studies reported reduced lung function in

adults with a history of pneumonia before the age of 2 years^{5,6} or lower respiratory tract illness before the age of 10 years.⁴ None of these studies satisfactorily assessed whether the effects of lower respiratory tract infection were related to a history of asthma or wheezing, and only one reported lung function in young adults,⁴ when the effects of confounding factors would be expected to be small.

In a study of ventilatory function in a nationally representative sample of adults followed from birth, we concluded that the association between childhood wheezing and adult morbidity might be caused by progressive pulmonary changes due to chronic asthma.⁷ Here we present data on the effects of childhood pneumonia and whooping cough on ventilatory function in the same cohort at the age of 34 or 35 years, and assess whether such effects are due to wheezing and other factors associated with lower respiratory tract infection and lung function during childhood.

METHODS**Study Subjects**

The British National Child Development Study (1958 cohort) is a longitudinal study of all the people in England, Scotland, and Wales who were born during the same week in March 1958. The cohort was followed up at the ages of 7, 11, and 16 years by means of parental interviews and examinations conducted by school medical officers, and at the ages of 23 and 33 years by means of interviews. Further details of the follow-up and our subsequent study of ventilatory function at the age of 34 or 35 years are presented elsewhere.^{7,8} In brief, of 18,559 subjects, complete data were available at birth and at all five follow-up evaluations for 5470 subjects. From these, we selected all those with a history of asthma, wheezing, or wheezy bronchitis (collectively termed "wheezing" henceforth) at any postnatal follow-up, all those with a history of pneumonia by the age of seven years (total, 2174 subjects), and a random sample (approximately 20 percent) of the remainder (706 subjects). After we excluded 265 subjects because they lived in remote areas, we asked 2615 to participate in this study between August 1992 and July 1993. After one reminder, 1875 subjects (72 percent) responded, 1594 (61 percent) agreed to take part, and 1449 (55 percent) were examined. The histories of pneumonia and whooping cough were determined by inquiry at the age-seven follow-up visit, when parents were asked whether their children had "ever had pneumonia" (and if so, at what age) and whether the child had "ever had whooping cough" (though

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not at what age). The subjects in this study are the same as those in our previous report, except that the subjects with a history of pneumonia are now included in the analysis.⁷ The study was approved by the St. George's Hospital Ethical Committee and by the 215 ethics committees in the health districts where the examinations were performed.

Measurements of Ventilatory Function

As previously reported,⁷ the subjects were examined in their homes by 1 of 20 trained nurses. They were asked about past and current respiratory symptoms, cigarette smoking, and indoor environmental exposures. After their height was measured, spirometry (Vitalograph, Buckingham, United Kingdom) was performed, according to the recommendations of the American Thoracic Society,⁹ before and 20 minutes after inhalation of 400 μ g of dry-powder albuterol (Ventolin). The spirometers were calibrated weekly. The highest forced expiratory volume in one second (FEV₁) and the highest forced vital capacity (FVC) from each set of spirometry were selected. The analyses were restricted to the 1392 subjects (96 percent) who had satisfactory spirometry both before and after they inhaled albuterol. Of these, 1060 had a history of wheezing, 193 had a history of pneumonia (of whom 136 also had a history of wheezing), and 275 had no history of either wheezing or pneumonia by the age of seven years. There were 215 subjects with a history of whooping cough by the age of seven (of whom 183 also had a history of wheezing) and 300 with no history of either wheezing or whooping cough. There were 38 subjects who had histories of both pneumonia and whooping cough.

Statistical Analysis

Tabulations and multiple regression models were calculated by the FREQ and GLM procedures of the Statistical Analysis System.¹⁰ Measurements of FEV₁ and FVC and the ratio of FEV₁ to FVC were used as outcome variables in multiple regression mod-

els that adjusted for observer, month of test, sex, height, and smoking history. No adjustment for age was necessary, since all subjects were 34 or 35 years old.¹¹ "Observer" and "month of test" were fitted as categorical variables. The adjustment for sex and height involved fitting separate intercepts and slopes for each sex. The data fitted a linear model. The terms for smoking included categorical variables (the subject never smoked, was a former smoker, or was a current smoker) and continuous variables (the number of cigarettes currently smoked daily).

Dummy variables were used to compare the ventilatory function of subjects who had a history of pneumonia or whooping cough with that of those without such a history. The subjects were further categorized into three groups according to their history of wheezing at any follow-up visit: no history of wheezing, wheezing in the past, or present wheezing (i.e., in the year before examination). The group with a history of pneumonia was subdivided according to the age at the time of the first episode of pneumonia (under two years or two to seven years), as reported by the parents. The regression coefficients from these models represent the adjusted difference in mean lung function between the group with a history of pneumonia or whooping cough and the group without such a history. All P values are two-tailed.

A second model also included both the variables from the main analysis (observer, month of test, sex, height, and smoking history) and the variables that in univariate analyses were significantly associated with a history of pneumonia or whooping cough or with lung function. These variables were the region of birth, birth order, own social class, father's social class, whether there was maternal smoking during pregnancy, whether there was exposure to tobacco smoke at home or at work, birth-weight quartile, height quartile at the age of seven years, duration of breast-feeding, whether gas was used for cooking currently and during childhood, and whether there was occupational exposure to dust. Adjustment was also made for a history of pneumonia in the whooping-cough analysis, and for a history of whooping cough in the pneumonia analysis. This "fully adjusted" model was based on 1151 subjects (83 percent) for whom complete data for all variables were available.

RESULTS

Representativeness of Subjects and Comparison of Self-Reported and Parental Histories

We compared the 1392 subjects included in the analysis with the 1223 subjects not examined or excluded because of inadequate spirometry (Table 1). There were no significant differences in sex distribution or in the proportions with a history of pneumonia or whooping cough. The subjects who had been examined were more likely to have had a history of wheezing and less likely to have smoked.

Of the subjects reported by their parents to have had pneumonia or whooping cough by the age of 7 years, only 106 of 193 (55 percent) and 77 of 215 (36 percent), respectively, reported such a history themselves on inquiry at the age of 34 or 35 years. Conversely, 53 of 159 (33 percent) and 74 of 151 (49 percent) subjects who reported having had pneumonia or whooping cough, respectively, had not been reported by their parents to have had such a history by the age of seven years.

Effect of a History of Pneumonia on Adult Lung Function

The unadjusted mean FEV₁ and FVC values were 6 percent and 7 percent lower, respectively, in the 193 subjects with a history of pneumonia by the age

TABLE 1. CHARACTERISTICS OF THE SUBJECTS INCLUDED IN AND EXCLUDED FROM THE ANALYSIS.

CHARACTERISTIC	SUBJECTS INVITED TO PARTICIPATE (N = 2615)	SUBJECTS INCLUDED IN ANALYSIS (N = 1392)	SUBJECTS EXCLUDED FROM ANALYSIS (N = 1223)*	P VALUE†
	number (percent)			
Male sex	1318 (50)	695 (50)	623 (51)	0.63
Pneumonia by age 7	350 (13)	193 (14)	157 (13)	0.48
Whooping cough by age 7	392 (15)	215 (15)	177 (14)	0.52
Asthma or wheezy bronchitis by age 7	1021 (39)	574 (41)	447 (37)	0.02
Asthma or wheezing starting after age 7	864 (33)	486 (35)	378 (31)	0.03
No history of asthma or wheezing	730 (28)	332 (24)	398 (33)	<0.001
Manual occupation at age 23‡	986 (38)	493 (35)	493 (40)	0.01
Smoker at age 23	1059 (40)	504 (36)	555 (45)	<0.001

*The subjects excluded were those who were invited to participate but were not examined because of a lack of response, refusal, pregnancy, or failed contact, plus those excluded from the basic regression model because of inadequate spirometric results.

†P values are for the comparisons between subjects included in and those excluded from the analysis.

‡"Manual occupation" is an index of social class in Great Britain.

TABLE 2. UNADJUSTED RESULTS OF SPIROMETRY IN SUBJECTS WITH AND THOSE WITHOUT A HISTORY OF PNEUMONIA OR A HISTORY OF WHOOPING COUGH BY THE AGE OF SEVEN YEARS.*

MEASUREMENT OF LUNG FUNCTION	SUBJECTS WITH PNEUMONIA BY AGE 7 (N=193)	SUBJECTS WITHOUT PNEUMONIA BY AGE 7 (N=1199)	SUBJECTS WITH WHOOPING COUGH BY AGE 7 (N=215)	SUBJECTS WITHOUT WHOOPING COUGH BY AGE 7 (N=1177)
FEV ₁ (liters)				
Before albuterol	3.430±0.744	3.649±0.763	3.444±0.764	3.651±0.740
After albuterol	3.521±0.754	3.756±0.758	3.550±0.748	3.755±0.760
FVC (liters)				
Before albuterol	4.247±0.901	4.570±0.929	4.291±0.887	4.568±0.933
After albuterol	4.261±0.889	4.576±0.933	4.313±0.905	4.572±0.933
FEV ₁ :FVC (%)				
Before albuterol	80.9±6.5	80.0±6.9	80.4±6.9	80.1±6.8
After albuterol	82.8±6.4	82.4±6.2	82.6±6.4	82.4±6.2

*Plus-minus values are means ±SD. FEV₁ denotes forced expiratory volume in one second, and FVC forced vital capacity.

TABLE 3. ADJUSTED MEAN DIFFERENCES IN THE RESULTS OF SPIROMETRY BEFORE AND AFTER ALBUTEROL TREATMENT BETWEEN SUBJECTS WITH AND THOSE WITHOUT A HISTORY OF PNEUMONIA OR WHOOPING COUGH BY THE AGE OF SEVEN YEARS.*

VARIABLE	NO. OF SUBJECTS WITHOUT ILLNESS BY AGE 7	NO. OF SUBJECTS WITH ILLNESS BY AGE 7	DIFFERENCE IN FEV ₁	P VALUE	DIFFERENCE IN FVC	P VALUE	DIFFERENCE IN FEV ₁ :FVC	P VALUE
			milliliters		milliliters		percent	
Before albuterol								
Pneumonia	1199	193	-102±73	0.006	-173±70	0.001	+0.9±1.0	0.09
Age at onset								
<2 yr	1199	90	-46±103	0.38	-107±112	0.06	+0.9±1.4	0.20
2-7 yr	1199	89	-160±103	0.002	-241±111	<0.001	+0.8±1.4	0.26
Unknown	1199	14	-90±249	0.48	-153±270	0.27	+0.9±3.4	0.62
Whooping cough	1177	215	-41±70	0.25	-81±76	0.04	+0.4±1.0	0.36
After albuterol								
Pneumonia	1199	193	-113±69	0.001	-161±78	<0.001	+0.4±0.9	0.42
Age at onset								
<2 yr	1199	90	-59±109	0.29	-72±122	0.24	-0.1±1.5	0.91
2-7 yr	1199	89	-157±109	0.005	-209±121	<0.001	+0.2±1.5	0.78
Unknown	1199	14	-123±280	0.39	-204±313	0.20	+1.0±3.8	0.61
Whooping cough	1177	215	-35±66	0.29	-61±75	0.11	+0.3±0.9	0.56

*The results are adjusted mean differences (±95 percent confidence limits) between the subjects with a history of illness and those without such a history. The results are adjusted throughout by multiple regression for observer (20 categories), month of test (12 categories), sex, height, smoking history (3 categories), and number of cigarettes currently smoked daily. FEV₁ denotes forced expiratory volume in one second, and FVC forced vital capacity.

of seven years than in those without such a history, with no significant effect of albuterol observed (Table 2). After adjustment, a history of pneumonia was associated with a significantly reduced FEV₁ and FVC, with no change in the FEV₁:FVC ratio (Table 3). These effects were similar for men and women separately (Table 4). There were no significant differences between the sexes in the effect of a history of pneumonia. The deficit in FEV₁ and FVC associated with such a history was not reduced by albuterol (Table 3). The age at the time of the first ep-

isode of pneumonia was known for 179 subjects. There was a larger reduction in FEV₁ and FVC in the subjects who had pneumonia between the ages of two and seven years than in those who had it earlier (Table 3), although these differences according to the age of onset were not statistically significant (FEV₁, P=0.12; FVC, P=0.08).

The deficit associated with a history of pneumonia was evident within each category of wheezing, being marked in the subjects with either no history of wheezing or current wheezing (Table 4), and again

was not reduced after treatment with albuterol. The estimated effect of a history of pneumonia on FVC in subjects who had never wheezed was a decrease of 197 ml (95 percent confidence limits, ± 152), and in those with current wheezing it was a decrease of 267 ml (95 percent confidence limits, ± 128). Reductions in FEV₁ and FVC among those with a history of pneumonia were found consistently in all smoking categories and were not confined to subjects who had had low birth weights.

Effect of a History of Whooping Cough on Adult Lung Function

The unadjusted mean FEV₁ and FVC values were each 6 percent lower in the 215 subjects with a history of whooping cough by the age of seven years than in those without such a history, with the differences persisting after treatment with albuterol (Table 2). After adjustment, the effects of a history of whooping cough were less than those of a history of pneumonia (Table 3). The only significant association was with a reduced FVC (Table 5), an effect not diminished by albuterol. In contrast to the subjects with a history of pneumonia, there was a significant difference according to sex in the subjects with a history of whooping cough, with effects largely confined to men (tests for modification of effect by sex: FEV₁, $P=0.05$; FVC, $P=0.006$). There was no suggestion of any difference in effect between the subjects with and those without a history of wheezing (Table 5). Differences in the effect of a history of whooping cough between the categories of smoking and birth weight were not significant.

Effect of Potentially Confounding Variables

The inclusion of potentially confounding variables in the fully adjusted model led to estimates of deficits in lung function that were almost identical to those from the basic model in the same 1151 subjects (Tables 4 and 5).

DISCUSSION

We found that having pneumonia by the age of 7 years is associated with reduced ventilatory function at the age of 34 or 35 years and that this association is independent both of a history of asthma or wheezing and of potentially confounding factors associated with lower respiratory tract infection. By contrast, having whooping cough before the age of seven years is not generally associated with reduced lung function.

Previous studies have suggested that lower respiratory tract infection during childhood is associated with a reduction in lung function later in life.¹⁻³ Studies of children previously hospitalized for infections with specific pathogens, such as respiratory syncytial virus¹¹⁻¹³ or *Mycoplasma pneumoniae*,¹⁴ have found reduced lung function. However, many such

studies were small, the subjects were not followed to adulthood, and there probably were biases due to diagnostic and referral patterns and in the selection of control subjects. Population studies have reported lung function in adults, with retrospective ascertainment of lower respiratory tract infection,^{15,16} but as we have shown here and elsewhere,⁷ such ascertainment is highly unreliable. Only three previous studies assessed adult lung function with independent ascertainment of respiratory tract infection during childhood. In two of these studies, FEV₁ and FVC were reduced in men 59 to 74 years of age with a history of childhood pneumonia or bronchitis as determined by a review of nursing records from about 1920.^{5,6} Including bronchitis with pneumonia may have led to the inclusion of asthmatic episodes in one study,⁵ and in the other only 13 men with a history of pneumonia were reported.⁶ The 1946 British birth-cohort study collected data on lower respiratory tract infection every two years from birth.⁴ The occurrence of respiratory illness by the age of two years was not associated with a reduced peak expiratory flow rate in adulthood after control for confounding factors.¹⁷

The strengths of our study are its population base and the ascertainment of pneumonia and whooping cough on the basis of information from parents when the subjects were seven years old. The prospectively obtained data indicate that the effect of childhood pneumonia is independent of such potential confounding factors as whether the parents smoked,¹⁸⁻²³ family size,^{4,24} birth weight,²⁵⁻²⁷ and whether gas was used for cooking.^{19,28,29} Indeed, the adjustment for multiple confounding factors tended to increase the effects of histories of pneumonia and whooping cough. Residual confounding by unmeasured factors was therefore unlikely. Nevertheless, the study has potential inadequacies. The ascertainment of pneumonia and whooping cough by means of interviews with the mothers when the subjects were seven years old may have been subject to diagnostic inaccuracy and recall bias.³⁰ Although no diagnostic validation was done, we considered parents unlikely to have reported pneumonia or whooping cough unless the illness had been so designated by a doctor. The response rate of 55 percent is also a source of concern, although important selection bias was unlikely, because the subjects examined were representative with respect to sex and the history of pneumonia or whooping cough.

We found, in agreement with others,^{5,6} that childhood pneumonia was associated with deficits in both FEV₁ and FVC, with no change in the FEV₁:FVC ratio — i.e., with a reduction in lung size rather than a narrowing of the airway. The effect was similar in both sexes, although others have suggested a greater effect on men.^{6,31} The size of the adjusted deficit as shown by spirometry at the age of 34 or 35 years in

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TABLE 4. ADJUSTED DIFFERENCES IN THE RESULTS OF SPIROMETRY BEFORE ALBUTEROL TREATMENT BETWEEN SUBJECTS WITH AND THOSE WITHOUT A HISTORY OF PNEUMONIA BY THE AGE OF SEVEN YEARS.

CATEGORY	NO. OF SUBJECTS WITHOUT A HISTORY OF PNEUMONIA BY AGE 7	NO. OF SUBJECTS WITH A HISTORY OF PNEUMONIA BY AGE 7	DIFFERENCE IN FEV ₁ * P VALUE		DIFFERENCE IN FVC* P VALUE		DIFFERENCE IN FEV ₁ :FVC* P VALUE	
			DIFFERENCE IN FEV ₁ * milliliters	P VALUE	DIFFERENCE IN FVC* milliliters	P VALUE	DIFFERENCE IN FEV ₁ :FVC* percent	P VALUE
All subjects	1199	193	-102±73	0.006	-173±70	0.001	+0.9±1.0	0.09
Men	611	84	-106±126	0.10	-171±135	0.01	+0.7±1.5	0.35
Women	588	109	-98±81	0.02	-171±89	<0.001	+1.0±1.4	0.14
Never wheezed	275	57	-155±122	0.01	-197±152	0.01	+0.3±1.5	0.67
Past wheezing	489	62	-41±128	0.53	-75±147	0.32	+0.3±1.6	0.69
Current wheezing	435	74	-119±133	0.08	-267±128	<0.001	+2.0±2.0	0.04
Basic model†	1003	148	-89±81	0.03	-155±87	<0.001	+0.8±1.1	0.18
Fully adjusted model‡	1003	148	-92±82	0.03	-159±88	<0.001	+0.8±1.1	0.18

*The values shown are adjusted mean differences (±95 percent confidence limits) between the subjects with a history of pneumonia and those without such a history. The results are adjusted throughout by multiple regression for observer (20 categories), month of test (12 categories), sex, height, smoking history (3 categories), and the number of cigarettes currently smoked daily ("basic model"). FEV₁ denotes forced expiratory volume in one second, and FVC forced vital capacity.

†This analysis of the basic model was restricted to subjects included in the fully adjusted model.

‡The model was further adjusted for region of birth (3 categories), birth order (4 categories), father's social class (6 categories), maternal smoking during pregnancy (4 categories), duration of breast-feeding (3 categories), birth-weight quartiles, height quartiles at the age of seven, current social class (6 categories), tobacco-smoke exposure at home (2 categories) and at work (2 categories), the use of gas for cooking now (2 categories) and in childhood (2 categories), occupational exposure to dust or fumes (2 categories), and history of whooping cough.

TABLE 5. ADJUSTED DIFFERENCES IN RESULTS OF SPIROMETRY BEFORE ALBUTEROL TREATMENT BETWEEN SUBJECTS WITH AND THOSE WITHOUT A HISTORY OF WHOOPING COUGH BY THE AGE OF SEVEN YEARS.

CATEGORY	NO. OF SUBJECTS WITHOUT A HISTORY OF WHOOPING COUGH BY AGE 7	NO. OF SUBJECTS WITH A HISTORY OF WHOOPING COUGH BY AGE 7	DIFFERENCE IN FEV ₁ * P VALUE		DIFFERENCE IN FVC* P VALUE		DIFFERENCE IN FEV ₁ :FVC* P VALUE	
			DIFFERENCE IN FEV ₁ * milliliters	P VALUE	DIFFERENCE IN FVC* milliliters	P VALUE	DIFFERENCE IN FEV ₁ :FVC* percent	P VALUE
All subjects	1177	215	-41±70	0.25	-81±76	0.04	+0.4±1.0	0.36
Men	608	87	-123±125	0.05	-215±134	0.002	+1.0±1.5	0.20
Women	569	128	+20±76	0.60	+21±84	0.63	+0.0±1.3	0.94
Never wheezed	300	32	-40±159	0.62	-52±197	0.60	+0.3±2.0	0.74
Past wheezing	453	98	-35±104	0.52	-91±118	0.13	+0.8±1.3	0.24
Current wheezing	424	85	-84±126	0.19	-93±123	0.14	-0.5±1.9	0.62
Basic model†	974	177	-39±76	0.32	-62±81	0.13	+0.1±1.0	0.86
Fully adjusted model‡	974	177	-41±77	0.29	-61±83	0.15	+0.0±1.1	0.99

*The values shown are adjusted mean differences (±95 percent confidence limits) between the subjects with a history of whooping cough and those without such a history. The results were adjusted throughout by multiple regression for observer (20 categories), month of test (12 categories), sex, height, smoking history (3 categories), and the number of cigarettes currently smoked daily ("basic model"). FEV₁ denotes forced expiratory volume in one second, and FVC forced vital capacity.

†This analysis of the basic model was restricted to subjects included in fully adjusted model.

‡The model was adjusted further for region of birth (3 categories), birth order (4 categories), father's social class (6 categories), maternal smoking during pregnancy (4 categories), duration of breast-feeding (3 categories), birth-weight quartiles, height quartiles at the age of seven, current social class (6 categories), tobacco-smoke exposure at home (2 categories) and at work (2 categories), the use of gas for cooking now (2 categories) and in childhood (2 categories), occupational exposure to dust or fumes (2 categories), and history of pneumonia.

our study was similar to that found at the age of 59 to 70 years for the effects of bronchitis and pneumonia in infancy.⁵ We were unable to confirm a greater effect of infection at a younger age^{6,31}; having pneumonia between the ages of two and seven years was associated with a deficit equal to or greater than having it before the age of two years, in broad agreement with Barker et al.⁵ Others have found no effect of lower respiratory tract infection before the age of two on lung function in adults or children.^{17,32}

Previous studies have shown no effect of whooping cough on later lung function^{33,34} or bronchial reactivity.³⁵ The effects of a history of whooping cough in our study were much less marked than those of a history of pneumonia. The only significant association, with reduced FVC in men, is difficult to interpret and may represent a chance finding in multiple subgroup comparisons.

The association between childhood pneumonia and adult lung function might arise through one or more mechanisms. First, the reduction of lung function probably reflects a loss of attained lung function rather than an accelerated decline during adulthood, although attenuation of the plateau phase in early adult life is possible.³⁶ The effect of pneumonia is not exerted through an association with wheezing. The deficit is not obstructive, is not reversed by albuterol, and is independent of a prospectively determined history of wheezing. The possibility of confounding by smoking can be excluded. Although data on the duration of smoking were not available, the cohort was relatively young, adjustment for self-reported smoking at the ages of 16 and 23 years did not affect the results, and the effects of a history of pneumonia on lifetime nonsmokers were very similar to those in the fully adjusted model. The effect of a history of pneumonia was also independent of other potential confounding factors.

The question that remains is whether pneumonia during childhood directly causes loss of adult lung function or whether pneumonia is more common in children who have poorer lung function before the disease. We cannot answer this question, but our finding that the age at which a child has pneumonia does not affect the deficit supports the latter hypothesis, since alveolar multiplication is nearly complete by the age of two years³⁷ and early lung injury might be expected to lead to a greater loss of lung function. Indirect evidence of birth-month variations in the incidence of early lower respiratory tract infection and subsequent ventilatory function also argues against direct lung damage from early pneumonia.³⁸ Recent studies suggest that lower respiratory tract illness may indeed be more likely in those with preexisting deficits in lung function,^{39,40} although lung function before the illness was lower only in the subjects in whom wheezing respiratory illness developed, as opposed to nonwheezing respiratory illness.⁴⁰

In conclusion, our study provides evidence of a direct association between pneumonia during childhood and reduced lung function in adulthood. This reduction is independent of both a history of wheezing and other confounding factors. It remains unclear whether pneumonia causes the deficit in lung function or whether pneumonia is more common among children who have poorer lung function before the disease.

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