Pulmonary Function Tests in Acute Bronchitis: Evidence for Reversible Airway Obstruction

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Acute bronchitis is a common syndrome characterized by upper respiratory tract infection accompanied by productive cough in persons without chronic lung disease. As a first step in investigating the potential role of pulmonary airflow disturbances in acute bronchitis, 27 adult patients with acute bronchitis performed serial pulmonary function tests and daily peak flow measurements and completed daily symptom diaries. Eleven patients (40 percent) had a forced expiratory volume of the first second (FEV_1) at entry less than 80 percent of predicted. Mean FEV_1, forced midexpiratory flow rate (FEF_{25-75}), and peak flow measures showed steady improvement over the five-week period. Differences between initial and final flow rates were statistically significant. These changes were particularly evident when two groups were created by stratifying by "abnormal" ($FEV_1 \leq 80$ percent predicted) and "normal" ($FEV_1 > 80$ percent predicted) initial FEV_1. Total duration of cough and subjective ratings of cough severity were not predicted by initial FEV_1, but work absence was significantly higher in the abnormal group. The finding of reversible airway obstruction suggests a role for bronchospasm in many cases of acute bronchitis and calls for further research regarding proof of rapid reversibility and treatment with bronchodilators.

Acute bronchitis is a clinical syndrome characterized by cough and sputum production accompanied by upper respiratory tract and systemic manifestations of infection. The duration of the syndrome is considerable, with one half of the patients coughing for three weeks and one fourth continuing to cough after one month.[1] It is a common illness, consistently ranking as one of the most frequently made diagnoses by primary care physicians.[2–6] Although the outcomes are uniformly good, cumulative morbidity and expense from this common disease are high.[7]

Acute bronchitis occurs in persons without chronic lung disease; it is distinct in this regard from acute exacerbations of chronic bronchitis. It has generally been considered an infectious disease with edema of the mucous membranes, destruction of respiratory epithelium, and diminished mucociliary function.[8]

Submitted, revised, April 16, 1987.

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Several studies have documented the association of various viruses with the syndrome of acute bronchitis. Rhinovirus, respiratory syncytial virus, parainfluenza virus, influenza virus, adenovirus, and enterovirus have all been found in conjunction with upper respiratory tract infection and productive cough in the absence of pneumonia.[8–11] Five to 10 percent of acute bronchitis cases in college students,[12,13] young airmen,[14] and patients in a prepaid health plan[15] were associated with laboratory evidence of mycoplasma infection. Although potentially pathogenic bacteria can occasionally be cultured from the sputum of a small proportion of acute bronchitis patients,[16,17] the distribution of organisms is not strikingly different from that found in the oropharyngeal flora of normal persons.[18] Thus, most observers have considered viruses to be the significant pathogens in this disease.

Previous studies have demonstrated the effect of viral infection on airways reactivity. Uncomplicated upper respiratory tract infections, particularly those due to rhinovirus, respiratory syncytial virus, and influenza virus, precipitate an abnormal response to inhaled challenge tests for as long as several weeks.[19–23]

Some have suggested that the prolonged and bothersome cough in acute bronchitis may be the result of bron-

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chospasm. Hallett and Jacobs,[24] for example, found that two thirds of recurrent acute bronchitis sufferers referred to their allergy clinic had asthma. A retrospective cohort study found that 16 percent of acute bronchitis patients in a primary care practice were diagnosed with asthma in the five years subsequent to their bronchitis episode; only 1.7 percent of controls were similarily diagnosed.[25] Perhaps acute bronchitis represents temporary, symptomatic bronchospasm in the absence of clinical conditions that would usually be labeled asthma.

The current study was undertaken to determine whether an obstructive pattern on pulmonary function tests might suggest occult bronchospasm in nonasthmatic patients with acute bronchitis. Bronchodilator and inhalation challenge tests were not done in this descriptive study.

METHODS

Selection of Subjects

The study was conducted at the University of Missouri–Columbia in the Family Medical Care Center, a primary care facility staffed by faculty and resident family physicians and nurse practitioners.

Patients were referred to the investigator at the discretion of the primary providers, who were asked to refer any patient with the diagnosis of acute bronchitis to the study. The investigator then interviewed the patient to ensure eligibility. Patients were considered for admission to the study if they were aged 21 to 60 years and had a productive cough associated with an upper respiratory tract infection. Exclusion criteria included chronic heart disease, temperature greater than 39.5 °C, history of pneumonia in the past two months, history of asthma except childhood asthma, physical examination or radiographic evidence of pneumonia, and chronic bronchitis and emphysema. Laboratory tests and radiographic studies were done at the discretion of the primary provider and were not routine parts of the study. No restrictions were placed on medications or other treatment.

Design

Data were collected at the patient's first visit for acute bronchitis and at visits one, three, and five weeks later. The standardized protocol recorded age, sex, smoking status, duration of cough, respiratory and systemic symptoms, vital signs, physical examination findings, and medications prescribed at the initial visit.

Subjects recorded in a symptom diary a daily ten-point subjective assessment of cough severity and overall health and also whether work or school was attended.

Pulmonary Function and Peak Flow Tests

At the initial visit and at visits one, three, and five weeks later, pulmonary function tests were performed using a Spirometrics model 2453 spirometer. Each subject received a standard set of instructions; the best of three efforts was recorded for each visit.

In addition, each patient received an Assess peak flow meter as well as spoken and written instruction in its use. Each was observed by the investigator or research assistant until an adequate technique was assured. The best of three peak flows was recorded each evening in the symptom diary.

Data Analysis

Mean values were calculated for forced expiratory volume of the first second (FEV_1), forced midexpiratory flow rate (FEF_{25-75}), peak flow rates, days of work missed, cough duration, and subjective ratings of cough and overall well-being. Correlation coefficients were derived relating FEV_1 at the initial and one-week visits to subjective scores of cough severity and overall well-being at day 1 and day 7.[26] Differences between initial and final lung function measurements were statistically compared using *t* tests.[26] These measurements were also plotted against time to provide a visual display of serial pulmonary function.

Two subgroups were retrospectively defined using initial FEV_1 values to derive "normal" and "abnormal" groups. Group A was defined by $FEV_1 \leq 80$ percent of predicted and group B by $FEV_1 > 80$ percent of predicted at the first visit. Serial tests of pulmonary function and ratings of cough and overall health were compared for these two subgroups as were differences in days of work missed and total duration of cough.

The outcome variables and pulmonary function tests were also evaluated after stratifying by factors that might be expected to affect outcome: cigarette smoking, prescription of bronchodilators, and a history of recurrent episodes of acute bronchitis.

RESULTS

Thirty-five patients were referred to the study, and 33 met the inclusion and exclusion criteria. Twenty-seven completed the study by having at least three of the four visits; 26 completed all four visits. Of the 8 patients not completing the study, 2 moved away, 4 others missed more than one follow-up visit, and 2 subsequently developed pneumonia and were therefore excluded.

The mean age of the patients at the initial visit was 32 years. There were nine men and 18 women. Forty percent were cigarette smokers. The mean duration of cough at

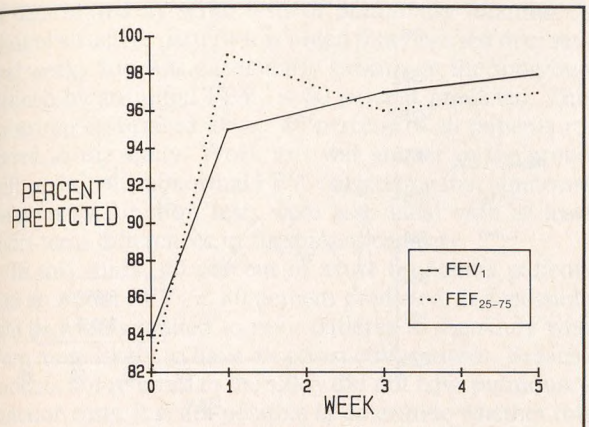

Figure 1. Mean percent predicted FEV_1 and FEF_{25-75} over a five-week period (n = 27)

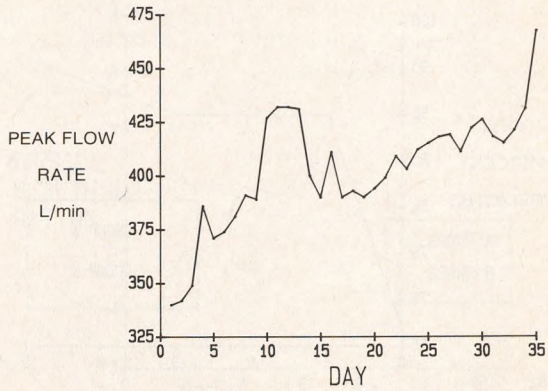

Figure 2. Mean daily home peak flow rates over a five-week period (n = 27)

the initial visit was 10.0 days, and 16 subjects had discolored sputum. Four patients gave family histories of asthma and two reported having asthma in childhood. Three patients had wheezes on physical examination. Six received bronchodilators, 15 reported previous histories of acute bronchitis, and 10 reported more than three previous episodes. These characteristics are similar to descriptions of acute bronchitis patients from previous studies.

The progression of mean FEV_1 and mean FEF_{25-75} over the five-week period for the whole group is shown in Figure 1. The progression of mean peak flow rates is displayed in Figure 2. The differences between initial and final mean values were FEV_1 84 percent vs 98 percent predicted ($P < .01$); FEF_{25-75} 82 percent vs 96 percent predicted ($P < .05$); peak flow 342 L/min vs 463 L/min ($P < .01$). The mean total duration of cough was 24.6 days and the mean amount of work missed was 1.5 days (Table 1).

The Pearson correlation coefficient between the cough severity rating on day 1 and initial FEV_1 was .27 and was of borderline significance. The correlation between overall well-being at seven days and FEV_1 at one week was .47 ($P < .01$). Other coefficients were less than .20.

Mean FEV_1 values in groups A and B are compared in Figure 3 over the five-week period. The difference between the initial and final FEV_1 findings in group A was 29.1 percentage points and in group B, 1.4 points ($P < .001$). In Figure 4, mean FEF_{25-75} is plotted for the two groups; the change in the mean for group A was 34.2 percentage points and for group B, 1.6 points ($P < .01$). Home peak flow curves over five weeks are shown in Figure 5; the change for the mean of group A was 113 L/min and for group B, 74 L/min ($P > .10$).

The progression in subjective ratings of cough severity is displayed in Figure 6, and in Figure 7 are the overall health ratings for the two groups over the first two weeks. There are no statistically significant differences and no trends are evident.

Patients in group A missed a mean of 2.3 days at work and those in group B missed 0.3 days ($P = .04$). The mean total duration of cough for group A was 21 days and for group B, 27 days ($P > .10$) (Table 1).

The data were also analyzed by stratifying for conditions that might be expected to affect outcome. Cigarette smokers were not more likely to be found in group A (Table 1), and when data were also stratified by presence or ab-

TABLE 1: CHARACTERISTICS OF THE WHOLE GROUP AND FOR TWO GROUPS STRATIFIED BY FORCED EXPIRATORY VOLUME AT ONE SECOND (FEV_1)

Characteristics	All Patients	Group A ($FEV_1 \leq 80\%$ predicted)	Group B ($FEV_1 > 80\%$ predicted)	P
Number	27	11 (41%)	16 (59%)	
Cough duration (days)	24.6	21	27	NS
Days off work	1.5	2.3	0.3	<.04
Cigarette smoker	11 (40%)	4 (36%)	7 (44%)	NS

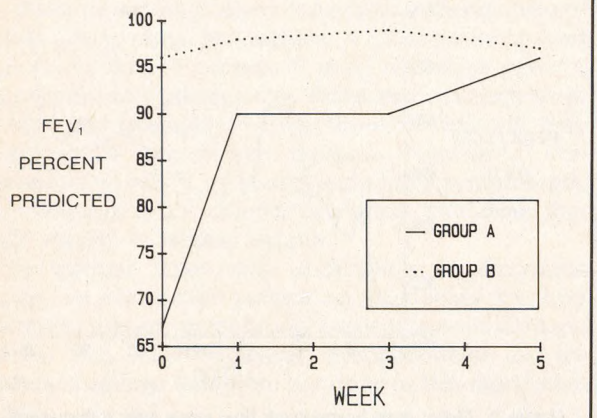

Figure 3. Mean percent predicted FEV_1 over a five-week period. Group A, initial $FEV_1 \leq 80$ (n = 11); group B, initial $FEV_1 > 80$ (n = 16)

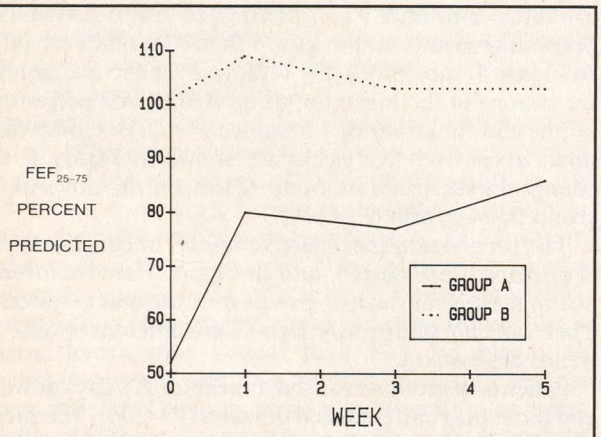

Figure 4. Mean percent predicted FEF_{25-75} over a five-week period. Group A, initial $FEV_1 \leq 80$ (n = 11); group B, initial $FEV_1 > 80$ (n = 16)

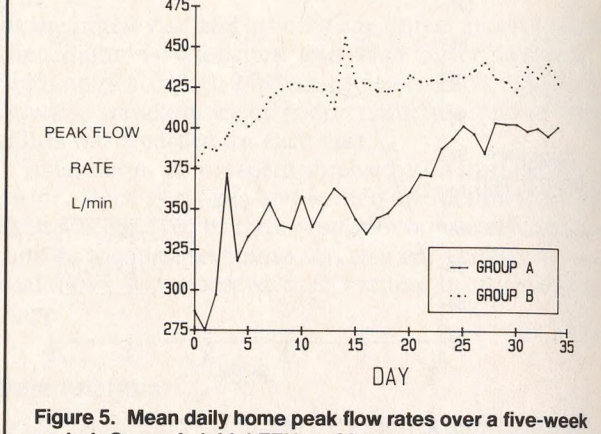

Figure 5. Mean daily home peak flow rates over a five-week period. Group A, initial $FEV_1 \leq 80$ (n = 11); group B, initial $FEV_1 > 80$ (n = 16)

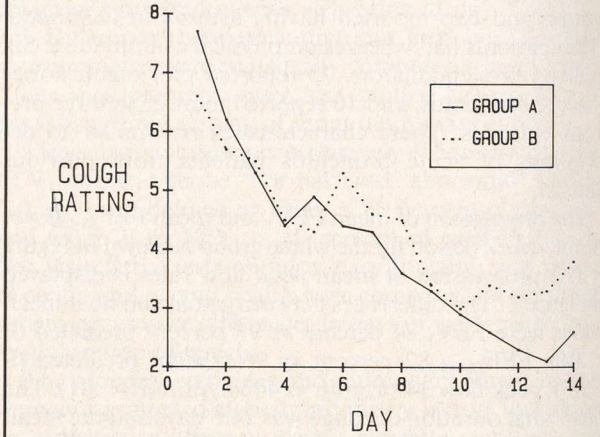

Figure 6. Mean daily subjective rating of cough severity over the first two weeks. Group A, initial $FEV_1 \leq 80$ (n = 11); group B, initial FEV_1 80 (n = 16)

sence of smoking, there was no finding that would suggest it as a risk factor for an obstructive pattern of prolonged duration or severity of cough or work absence.

The seven patients in group A who received no bronchodilators were compared with the 14 patients in group B who received no bronchodilators. The results were similar to that found when comparing the whole of group A with group B.

The ten patients who reported three or more previous episodes of acute bronchitis were then compared with the 17 who reported fewer than three previous episodes. A history of recurrent acute bronchitis did not predict a different pattern of progression of pulmonary function tests or duration or severity of cough.

DISCUSSION

The study was designed to investigate the association between acute bronchitis and pulmonary airflow obstruction

as determined by serial tests of pulmonary function. A clear obstructive pattern was noted that reversed over several weeks and was particularly striking in the subgroup defined by an initial $FEV_1 \leq 80$ percent predicted. This subgroup comprised about 40 percent of all patients referred to the study. Work loss was greater in the group with an initially abnormal FEV_1, suggesting that abnormal pulmonary function tests were associated with at least short-term differences in functional capacity.

In this study, 40 percent of acute bronchitis patients had an initial $FEV_1 \leq 80$ percent predicted. It is possible that providers tended to refer patients to the study who were more likely to have an obstructive pattern. Because patients not referred to the study did not have pulmonary function tests, it is not possible to determine whether this selection bias may have occurred. Even if there were a selection bias, the data would suggest that many patients with acute bronchitis exhibit an obstructive airway pattern.

Edema, mucous secretion, or poor effort on the part of some patients could be responsible for these findings. Bronchodilator testing and inhalation challenge tests were not a part of this descriptive study; therefore, the data cannot specify the cause of the obstructive pattern. Previous research has shown, however, that uncomplicated viral upper respiratory tract infections cause airway hyperreactivity to various inhalation challenges, including exercise, methacholine, and cold air.[19–23] Furthermore, two studies have shown an association between acute bronchitis and subsequent diagnosis of asthma.[24,25] These previous findings suggest, but do not prove, that bronchospasm may well be responsible for the obstructive pattern observed in this study.

Four patients in group A and two in group B received bronchodilators. The four patients in group A who received bronchodilators did not have a detectably superior clinical course than the seven who did not. Because the study was not designed to measure the effectiveness of bronchodilators and was therefore not randomized, no conclusions about the efficacy of bronchodilator therapy can be made.

The involvement of small and medium airways in these patients is highlighted by the differences in progression of FEV_1 and FEF_{25-75}. The FEF_{25-75}, usually thought to represent obstruction of smaller airways, was more depressed at the initial visit and did not return to normal at the end of four weeks. This finding is in keeping with the slower recovery of small airways in asthmatic patients.

The concept that the bothersome cough of acute bronchitis is related solely to airflow obstruction is not well supported by these data; the cough duration and cough severity ratings were nearly identical in groups with normal and abnormal pulmonary functions. It is of interest, however, that there was a correlation between FEV_1 and

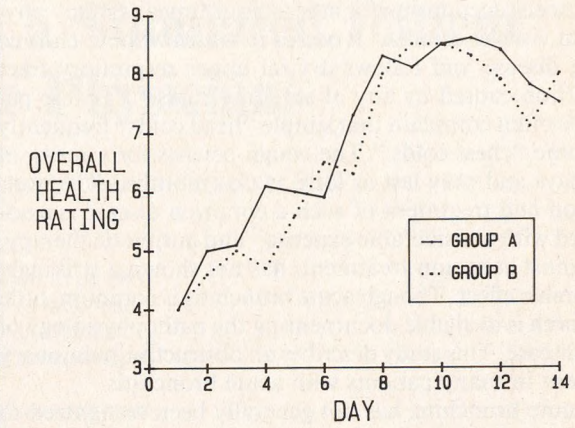

Figure 7. Mean daily subjective rating of overall health over the first two weeks. Group A, initial $FEV_1 \leq 80$ (n = 11); group B, initial $FEV_1 > 80$ (n = 16)

overall well-being at seven days. It is therefore still unclear whether these findings can determine a relationship between symptoms and respiratory obstruction.

Hallett and Jacobs'[24] finding of asthma in patients with recurrent acute bronchitis was not supported by this study; patients with recurrent acute bronchitis were not more likely to have an obstructive pattern.

Previous research has associated acute bronchitis with viral infection, viral infection with airway hyperreactivity, and acute bronchitis with subsequent diagnosis of asthma. There has been particular interest in the association of viral upper respiratory tract infection with bronchospasm that occurs even in patients not considered asthmatic. This phenomenon may be mediated by increased smooth muscle reactivity, sensitized vagal neuroreceptors, airway hyperpermeability, or airway sensitivity.[27] In children, this association has a described clinical correlate, so-called wheezing-associated respiratory tract infection (WARI).[28] WARI has been found in children not considered to have asthma, and there is reason to believe that WARI predisposes to chronic airways obstruction in adults.[29]

In adults, less evidence has documented clinical illness associated with virus-induced airway reactivity, except in asthmatics. Several studies document airway responsiveness in nonasthmatic adults,[19–23] but these subjects apparently did not have illness beyond a common cold. Studies in adults have identified unrecognized bronchospasm as a cause of chronic cough[30] and have demonstrated that wheezing is often not appreciated in asthmatics unless respiratory obstruction is moderately severe.[31] The syndrome called acute bronchitis in adults may be the clinical analog of WARI in childhood.

Acute bronchitis is an extremely common primary care diagnosis, accounting for at least four times as many physician visits as asthma.[2] It occurs in adults without chronic lung disease and follows a viral upper respiratory tract infection caused by any of several viruses.[8–11] These patients often complain that simple "head colds" frequently become "chest colds." The cough persists for a mean of 28 days and may last as long as two months.[1] The evaluation and treatment of such a common disease is associated with considerable expense,[7] and antibiotic therapy, the most common treatment, has not shown a strikingly favorable effect. Though acute bronchitis is common, little research is available documenting the pathophysiology of the disease. This study describes an obstructive pulmonary pattern in many patients with acute bronchitis.

Acute bronchitis has not generally been recognized to involve airway obstruction and is not often treated with bronchodilators. This study thus suggests a potential new therapy for a very common disease. Future research should include assessing the effect of bronchodilators on measures of pulmonary function and quality of life.

Acknowledgment

This work was supported by a grant from the Family Health Foundation of America.

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