Factors affecting the decline of ventilatory function in chronic bronchitis

ALASTAIR H CAMPBELL, COLIN E BARTER, JOHN M O'CONNELL, RICHARD HUGGINS

From the Department of Thoracic Medicine, Repatriation General Hospital, Heidelberg, and the Department of Statistics, La Trobe University, Bundoora, Victoria, Australia

ABSTRACT Ninety six middle aged male patients with chronic bronchitis with relatively well preserved ventilatory function who were resident in Queensland, New South Wales, or Victoria took part in a prospective study to determine the relationship of various factors to the rate of decline of the FEV₁. Thirty of the subjects withdrew, leaving 66 to be followed for four to six years. The mean rate of decline of the FEV₁ was 58.6 (SD 51.4) ml/year. The subjects' ventilatory responses to bronchodilator and to methacholine (measures of bronchial lability) were significantly related to each other and to sputum eosinophilia. With a linear model for the data on 57 patients who had methacholine and skin tests the rate of decline of the FEV₁ was found, after adjustment had been made for other variables, to be significantly related to State of residence, current smoking, response to bronchodilator, age, and occupational exposure to dust. Response to bronchodilator was interchangeable with response to methacholine. With the five variables in the model none of the following factors was related to the rate of decline of the FEV₁: FEV₁ on entry, FEV₁ % predicted normal, FEV₁/VC%, skin test reaction, occupation on entry, history of sinusitis and rhinitis, and height. When data from all 66 subjects were introduced into the model, in addition to the five significant individual variables (FEV₁/VC% × response to bronchodilator) was significantly related to the rate of decline of the FEV₁. Of these prognostic indices, response to bronchodilator was independent of the initial FEV₁, FEV₁/VC%, and FEV₁ % predicted. The difference between States, which was not explained by differences due to sampling or withdrawal of subjects, was due to a low rate of decline in Queensland.

Deterioration of the respiratory function of subjects with chronic bronchitis appears to be related to various social and environmental factors such as cigarette smoking,¹ atmospheric pollution,² occupational exposure to dust,³ and possibly place of residence. Also important are various factors such as age¹ and bronchial lability, measured either by the ventilatory response to methacholine or by the response to bronchodilator.⁴

As these and other factors may require consideration in the clinical management of patients with chronic bronchitis, we sought to determine their relative importance in a prospective study of a group

of patients with initially relatively well preserved ventilatory function.

Methods

The subjects in this investigation were drawn from ex-servicemen residing in the Australian States of Queensland, New South Wales, and Victoria who had presented to the Department of Veterans' Affairs with symptoms attributable to chronic bronchitis. With the intention of obtaining suitable volunteers for a prospective study of the rate of decline of the FEV₁, those likely to meet proposed selection criteria were contacted in 1967-8, by letter in New South Wales and Queensland and at outpatient review in Victoria, inviting them to participate; 55% in Queensland, 53% in New South Wales, and about 60% in Victoria agreed to be interviewed and assessed. Only a small minority met the following selec-

Address for reprint requests: Dr AH Campbell, Repatriation General Hospital, Heidelberg, Victoria 3077, Australia.

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tion criteria: (1) they fulfilled the Medical Research Council criteria for chronic bronchitis—that is, they had coughed sputum on most days during three consecutive months for at least two consecutive years and had no other relevant cause for cough or sputum⁵; (2) the one second forced expiratory volume (FEV₁) exceeded 60% of the predicted normal value, and FEV₁/vital capacity (VC) % was at least 50% and they had no other physical condition likely to interfere with respiratory function, such as cardiovascular disease, past pulmonary tuberculosis, or asthma. Asthma was identified if reversible episodes of dyspnoea or tightness of the chest with wheeze occurred at rest.

Of those assessed, 26 in Queensland, 26 in New South Wales, and 19 in Victoria met the selection criteria and agreed to participate. To increase the numbers a further group of 25 subjects meeting the selection criteria were recruited in Victoria in the same manner in 1974–5. Thus 96 subjects entered the study.

For the purpose of determining the rate of decline of the FEV₁ and to make other observations, a physician and technician visited each State initially in 1967–8 and thereafter at intervals of usually one year. The personnel of the visiting team changed after two years. For those subjects recruited in 1974–5 the final measurements were made by a third team. The personnel were all experienced and were instructed to use the same standard procedures and techniques. The same calibrated fast recording, water filled spirometer (LODE 10 litre) was used throughout. The FEV₁ and VC were measured after at least three closely reproducible slow expiratory traces had been obtained followed by three reproducible forced expiratory traces. The largest VC and FEV₁ were chosen for analysis. This procedure was repeated 15 minutes after the inhalation of isoprenaline sulphate delivered as a metered aerosol in a standard dose of 0.5 mg (Medihaler Iso Forte, Riker Laboratories Australia Pty Ltd, Sydney). These measurements were made at entry of the subject into the survey, and at approximately yearly intervals until 1979 or until the subject died or withdrew from the study. Ventilatory responsiveness to isoprenaline was obtained from the difference between the largest values for FEV₁ before and after isoprenaline inhalation. The average of the measurements for the first two visits was selected as the measure of the initial degree of reversibility of airway obstruction.

The subjects were free to withdraw from the investigation at any time and 30 (six from Queensland, nine from New South Wales, and 15 from Victoria) failed to co-operate adequately. Nine refused to co-operate after the initial examination and the

others withdrew or were withdrawn during the first three years of the investigation. The reasons for withdrawal of 25 subjects were inability to obtain leave from work, dislike of the procedures, and transfer to another region. Two subjects were unable to achieve reproducible results in the spirometric tests, and three developed illness other than bronchitis causing death or incapacity. This left 66 subjects (20 Queensland, 17 New South Wales, and 29 Victoria) available for determination of the rate of decline of the FEV₁. This was obtained in 59 subjects from the regression of at least four post-bronchodilator measurements of the FEV₁, at yearly or greater intervals during 4 to 6 years. Six subjects did not have an appropriate measurement during the fourth to sixth years and the annual decrease of FEV₁ was calculated from at least four measurements over a period of seven years. For a seventh subject, who died, the decrease was calculated from four measurements over 3.53 years.

The 66 subjects had other tests and assessments. Fifty eight consented to the measurement of the change in the FEV₁ after the administration of a standard dose of methacholine as described by Barter and Campbell.⁴

Sputum was obtained and smeared on to four glass slides and fixed before the subjects performed the methacholine provocation test. Satisfactory specimens from 55 of these 58 subjects were graded for eosinophilia.⁶

Skin tests were performed by using the prick method with control solution and four groups of allergens (CSL, D strength): (1) nine common grasses (combined in three groups of three); (2) animal danders—cat, dog, duck, and horse (individual doses); (3) house dust and housedust mite; (4) *Aspergillus fumigatus*. The size of the weals was recorded after 20 minutes. A weal of diameter greater than 3 mm was regarded as positive (after subtraction of the diameter size of the weal produced by the control).

At each visit detailed respiratory histories were obtained by means of a standard questionnaire, which provided information concerning occupation, exposure to dust or fumes, smoking habit, place of residence, and symptoms of rhinitis or sinusitis.

During their lifetime many of the subjects had changed their occupations. To simplify the examination we used only the occupation at the time of entry into the investigation, which was classified according to 4 and 7 point scales of status ranking of occupations in Australia.⁷ For the present purpose exposure to dust was regarded as having occurred if the subject described working in a dusty occupation for at least three months; usually exposure lasted years.

Rhinitis, allergic or non-allergic, was diagnosed

when there were episodes of increased watery nasal secretion. The diagnosis of sinusitis, before or during the investigation, was based on typical symptoms or a history of surgical intervention or both.

Smoking habits were assessed at each interview and the average number of cigarettes smoked daily during the survey was calculated for each person. For those who made their own cigarettes and for the few intermittent pipe smokers 1 g of tobacco was regarded as the equivalent of one cigarette.

STATISTICAL PROCEDURE

On the basis of simple correlations a linear model was fitted to the data to enable the variables that contributed to the rate of decline of FEV₁ to be determined. This procedure was not unlike the more usual stepwise regression methods, the main difference being the inclusion of qualitative factors such as State of residence. The general form of the model is given by

$$y = \mu + \alpha_i + \gamma_j + \beta_1 x_1 + \dots + \beta_n x_n + \epsilon,$$

where y is the rate of decline of FEV₁, μ is the overall or grand mean, α_i and γ_j represent differential effects due to the qualitative factors, $\beta_i x_i$, etc are the regressions on the quantitative variables $x_1, \dots, x_n$,⁸ and ϵ is the error.

Results

Characteristics of the subjects who were recruited and who withdrew or were followed are shown in table 1. Of those recruited in each State, there was no significant difference in FEV₁ % predicted normal or response to bronchodilator. In Victoria, where there were two intakes, the mean age was significantly greater than that of the New South Wales and Queensland subjects. Partly as a function of the age difference, the FEV₁ and FEV₁/VC% were greater in New South Wales than in Victoria.

Those withdrawing from the investigation were not significantly different from those followed apart from being taller and, in Victoria, younger.

The subjects who were followed were similar in each State, differing significantly only in age, the patients from Victoria being a little older (mean difference in age between patients from Victoria and those from Queensland 5.4 years; between Victoria and New South Wales 6.3 years; $p < 0.01$). All but five of these 66 patients were smokers on entry (Queensland 1, New South Wales 2, Victoria 2). Skin test reactions were positive in 29%. Fifty six per cent had worked at some time in a dusty environment, such work continuing after entry into the investigation in 26%. Thirty three per cent had a history of sinusitis and there was a lesser prevalence

of sinusitis in Victoria ($p < 0.05$) than in Queensland. The mean (SD) FEV₁ volume change after methacholine for 58 subjects was 0.521 (0.314) litres or 22.7% (17.6%).

THE ANNUAL DECLINE OF THE FEV₁

The annual decline of the FEV₁ could not be determined reliably for the 30 subjects withdrawn from the investigation. Nine refused to co-operate after the initial examination. Fifteen had a few measurements of FEV₁ during one to three years and another six had additional measurements after the survey period had ended. The paucity of measurements and the short and varying time spans make the results unreliable and unsuitable for analysis of covariance but they indicate that the subjects who withdrew in Queensland had about the same rate of decline of FEV₁ as those remaining in the investigation in that State, whereas in the other two States those who withdrew evidently had a greater rate of deterioration, although the magnitude cannot be relied on (table 2).

RELATIONSHIP BETWEEN ANNUAL DECREASE OF FEV₁ AND OTHER FACTORS

The rate of decline of the FEV₁ was significantly greater for those residing in New South Wales and Victoria than in Queensland (table 2). Correlation coefficients were calculated for the annual decrease of FEV₁ versus other characteristics for the 59 patients with identical follow up. A significant correlation was found between the annual decrease of the FEV₁ and 10 factors (table 3). No significant relationships were found between annual decrease of FEV₁ and any of the following: age, FEV₁ (on entry), FEV₁ % predicted normal, positive skin test reactions, rhinitis, occupation, treatment with bronchodilator.

Several of the variables were related. The ventilatory response to bronchodilator was significantly related to the ventilatory response to methacholine and both were inversely related to the FEV₁/VC%. There was a weak relationship between sputum eosinophilia and percentage response to either bronchodilator or methacholine (table 3).

ANALYSIS OF THE LINEAR MODEL

This part of the analysis was complicated by nine subjects who did not have certain tests (eight methacholine, one skin test), and initially these subjects were omitted. For the remaining subjects a stepwise procedure was used to fit a linear model to the data.

Of the 57 subjects, three had irregular follow up; the analysis was made with and without these irregular cases and produced similar results. The variables

Table 1 Characteristics of patients (values are means with standard deviations in parentheses)

	No of patients	Age (y)	Height (cm)	FEV ₁ (l)	FEV ₁ (% pred)	FEV ₁ /VC%	Bronchodilator response (% Δ FEV ₁)*
All States							
Recruited	96	52.5 (6.3)	172.5 (5.8)	2.70 (0.50)	84.1 (13.4)	67.0 (8.6)	5.5 (5.6)
Withdrawn	30	50.7 (5.8)	175.6 (5.4)	2.82 (0.57)	82.2 (14.0)	68.9 (9.5)	6.3 (5.2)
Followed	66	53.3 (6.4)	171.7 (6.4)	2.65 (0.46)	84.2 (14.6)	66.2 (8.0)	5.1 (5.6)
Queensland							
Recruited	26	52.1 (5.9)	170.9 (5.2)	2.57 (0.40)	81.3 (12.5)	68.5 (8.1)	7.0 (4.7)
Withdrawn	6	55.3 (5.6)	173.3 (0.8)	2.67 (0.43)	81.8 (13.8)	69.2 (9.3)	9.1 (3.7)
Followed	20	51.2 (5.7)	170.2 (5.8)	2.54 (0.40)	81.2 (12.4)	66.3 (8.0)	6.4 (4.9)
New South Wales							
Recruited	26	49.5 (5.1)	173.4 (7.0)	2.94 (0.53)	87.3 (13.5)	69.7 (9.1)	6.1 (5.6)
Withdrawn	9	47.7 (5.7)	175.2 (7.5)	3.13 (0.65)	88.1 (15.8)	73.4 (10.9)	6.9 (2.9)
Followed	17	50.4 (4.5)	172.4 (6.7)	2.84 (0.46)	86.9 (12.7)	67.7 (7.7)	5.7 (7.2)
Victoria							
Recruited	44	54.6 (6.6)	173.2 (5.9)	2.63 (0.50)	83.9 (13.7)	64.6 (8.0)	4.2 (5.5)
Withdrawn	15	50.6 (5.0)	176.8 (4.9)	2.69 (0.51)	78.9 (12.7)	65.9 (8.0)	4.7 (6.4)
Followed	29	56.6 (6.4)	171.3 (4.7)	2.61 (0.49)	86.5 (13.7)	64.0 (8.1)	4.3 (5.4)

State differences of recruited patients: Age: NSW v Vic, $p < 0.001$
 FEV₁: NSW v Vic, $p < 0.02$
 FEV₁VC%: NSW v Q, $p < 0.01$
 FEV₁VC%: NSW v Vic, $p < 0.02$
 Response to bronchodilator: Vic v Q, $p < 0.05$
 Age: Vic, $p < 0.005$
 Height: All States, $p < 0.001$; Q, $p < 0.05$; Vic, $p < 0.001$
 State differences of followed patients: Age: Vic v NSW and Vic v Q, $p < 0.005$

All other differences were not significant.

*Mean of first two measurements after inhalation of bronchodilator, except in the case of 10 patients who withdrew, who had one measurement only.

NSW—New South Wales; Q—Queensland; Vic—Victoria.

Table 2 Annual decrease of FEV₁ (values are means with standard deviations in parentheses)

State	Patients followed 4–6 y		Patients withdrawn*	
	n	Mean (SD) decrease of FEV ₁ (ml/y)	n	Mean (SD) decrease of FEV ₁ (ml/y)
All States	66	58.6 (57.4)	21	128.8 (107.2)
Queensland	20	25.8 (40.8)	5	24.8 (38.3)
New South Wales	17	65.8 (64.1)	7	194.0 (131.5)
Victoria	29	77.1 (55.0)	9	135.8 (67.3)

*See text. Nine followed for less than a year could not be included. The follow up was one to three years for 15; another six were persuaded to provide additional measurements after the survey had ended.

considered were: State of residence, age, response to methacholine (both volume and percentage change), FEV₁% of predicted normal, FEV₁, FEV₁/VC%, response to bronchodilator (both volume and percentage change), response to skin tests, history of sinusitis, occupational exposure to dust, current smoking habit, occupation (on a scale of 1–7), and height. The dependent variable was the annual rate of decline of the FEV₁ and the linear model was fitted with the help of the GLIM (generalised linear interactive modelling) statistical computing package.

The fitted model for this reduced data set consisted of five variables: State of residence, current smoking habit, response to bronchodilator (%), age, and exposure to dust. After adjustment had been made for other variables in the model each variable was found to be significantly related to the rate of

decline of the FEV₁. None of the other variables was significant after adjustment had been made for this model.

When the variable percentage response to bronchodilator was considered there were several competing variables—FEV₁/VC, FEV₁ volume change after bronchodilator, and both percentage and volume change in response to methacholine. When response to bronchodilator (%) was replaced by any of these variables the error sum of squares was somewhat higher; the responses to bronchodilator and methacholine were for all practical purposes, however, interchangeable; while with FEV₁/VC% in the model there was still a significant contribution from the response to bronchodilator.

As the variables for which there were missing observations (methacholine and skin test results) do not appear in the model given above, this model was

Table 3 Annual decrease of FEV₁ versus other factors

	Correlation coefficient	p Value	n
After bronchodilator:			
FEV ₁ volume change	0.346	< 0.01	59
FEV ₁ % change	0.361	< 0.01	59
After methacholine			
FEV ₁ volume change	0.368	< 0.01	54
FEV ₁ % change	0.478	< 0.001	54
Sputum eosinophilia grade	0.295	< 0.05	48
FEV ₁ /VC%	-0.493	< 0.001	59
Current cigarette smoking (No of cigarettes/day)	0.353	< 0.01	59
Exposure to dust	0.355	< 0.01	59
History of sinusitis	-0.305	< 0.05	59
Height	0.327	< 0.05	59
RELATIONSHIPS BETWEEN FACTORS			
FEV ₁ % change after bronchodilator v FEV ₁ % change after methacholine	0.487	< 0.001	54
FEV ₁ % change after bronchodilator v FEV ₁ /VC %	-0.432	< 0.001	59
FEV ₁ % change after methacholine v FEV ₁ /VC %	-0.378	< 0.01	54
FEV ₁ % change after methacholine v sputum grade of eosinophilia	0.325	< 0.05	48
% change after bronchodilator v sputum grade of eosinophilia	0.289	< 0.05	48

fitted to the entire data and further tests concerning the other variables were conducted. All the variables in the first model were found to be significant except for age, owing to interaction with FEV₁/VC%. This result was influenced by one subject who had a large difference between the predicted and actual rate of decline, who died soon after the study was completed. A robust regression procedure gave this subject small weight and we decided to simplify further analysis by omitting him. All the variables in the first model were then significantly related to rate of decline of the FEV₁.

The remaining tests carried out concerned the variables height, FEV₁, FEV₁/VC%, and FEV₁% of predicted normal. After adjustment had been made for the above model only FEV₁/VC% was found to be significantly related to the rate of decline of FEV₁. Further tests showed that there was a significant interaction between FEV₁/VC% and the percentage response to bronchodilator and after adjustment had been made for this and the model above there was no significant relationship with FEV₁/VC% (table 4).

Thus the final model was determined to consist of State of residence, current smoking habit, response to bronchodilator (%), FEV₁/VC% × response to bronchodilator (%), exposure to dust, and age. (The variable FEV₁/VC% × response to bronchodilator (%) represents an interaction between the two variables—that is, the effect of FEV₁/VC% on the rate of decline depends on the response to bron-

chodilator.) A robust regression procedure was used to check the parameter estimates and these robust estimates were quite close to those obtained by our methods with a few small discrepancies. Finally, the subject omitted from our analysis still showed a large deviation from this model. The regression equation for rate of decline and the six factors is shown in table 4b.

To obtain some idea of the contribution of each variable to the reduction in the sum of squares, the reduction due to that variable after adjustment for the others was divided by the total sum of squares and expressed as a percentage. Response to bronchodilator (%) accounted for 10% of the variance, State of residence 9%, current smoking habit 8%, exposure to dust 6%, FEV₁/VC% × percentage response to bronchodilator 6%, and age 5%. The degree of variance for each variable fitted singly was: State of residence 17%, current smoking habit 11%, percentage response to bronchodilator 9%, exposure to dust 6%, age 5%, and FEV₁/VC% × response to bronchodilator (%) 5%.

The adjusted mean rate of decline of the FEV₁ in the three States shows that the rate is significantly less for the Queensland residents than for the residents of the other two States (table 4). There was no difference between those who were smokers and those who were non-smokers on entry after adjustment for the model.

Discussion

The rate of decline of the FEV₁ of "normal" men in the United States has been reported as being 27⁹ and 28 ml/year¹⁰ for populations that excluded those with a history of respiratory disease but included smokers. Although the smoking histories are not detailed the prevalence of smoking in these populations was presumably less than for our patients.

For this reason and because our patients had chronic bronchitis, it was not surprising that overall (but not in the Queensland group) the rate of decline of FEV₁ was greater (59 ml/year) than "normal" values, falling within the range of 30–83 ml/year previously reported for groups of chronic bronchitic subjects.

We selected only subjects with minimal to moderate airflow limitation, to obtain a relatively uniform group in which to study the effects of other variants and to ensure that most survived the follow up period. We also aimed to avoid the paradoxical slowing of the rate of decline of the FEV₁ found in survivors with severe impairment of ventilatory function.¹¹

The previously demonstrated relationship between severity of impairment of function and subse-

Table 4 Analysis of the linear model A

Variable†	R ² of model‡	F of model§	Df	Variable F††	Df
State of residence	17	6.3**	2,62	7.2**	2,57
Current smoking	32	9.4**	3,61	11.8**	1,57
Response to bronchodilator (%)	46	12.7**	4,60	14.4**	1,57
FEV ₁ /VC% × response to bronchodilator (%)	52	12.5**	5,59	8.2**	1,57
Past exposure to dust	56	12.3**	6,58	9.0**	1,57
Age	61	12.6**	7,57	7.1**	1,57

† Variables given in order resulting from a stepwise procedure for the data after omission of the extreme observation discussed in the text.

‡ R² = 100 × (regression sum of squares)/(total sum of squares) for model consisting of current and preceding variables.

§ F value of model consisting of current and preceding variables.

†† F value for variable after adjustment for the remaining variables.

B Regression equation

Rate of decline of FEV₁ (ml/y) = -111
 - 32.37 (if Q resident)
 + 11.02 (if Vic resident)
 + 18.48 × response to bronchodilator (%)
 + 28.59 (if exposed to dust)
 + 1.712 × current smoking
 - 0.2393 × FEV₁/VC% × response to bronchodilator (%)
 + 2.213 × age

Estimate of standard deviation = 35.56
 Total sum of squares 184 300 (df 64)
 Error sum of squares 72 130 (df 57)
 R² = 61%

C Differences between the States of residence in the adjusted mean rate of decline of FEV₁ (ml/y)

NSW - Q	32.37**	(SE 12.30)
Vic - NSW	11.02	(SE 12.18)
Vic - Q	43.39**	(SE 12.37)

*Significant at 0.05 level.

**Significant at 0.01 level.

NSW—New South Wales; Q—Queensland; Vic—Victoria.

quent rate of decline of the FEV₁¹ was found in the present study for the FEV₁/VC% but not for the FEV₁% predicted, probably because of the relative uniformity of the group. This relationship was linked to and partly dependent on the response to bronchodilator.

The relationship between bronchial lability and rate of decline of the FEV₁ appeared to be independent of the initial geometry of the airways as the relationship persisted after adjustment had been made separately for FEV₁, FEV₁% predicted, and FEV₁/VC%. As in earlier studies,^{4,12} in assessing the rate of decline of the FEV₁, we preferred postbronchodilator to prebronchodilator values, as these are less likely to be subject to the cyclical variation of the reversible component of airflow limitation; but this refinement is unlikely to be critical. The present results confirm earlier, less comprehensive findings that bronchial reactivity to methacholine and ventilatory response to a bronchodilator are related to long term deterioration of ventilation.^{4,12} It is not surprising that the two different measures of bron-

chial lability were shown to be related to each other as both can be increased together, as in asthma. Fletcher *et al*¹ found that asthmatic subjects had a significantly greater rate of decline of the FEV₁ than the average for all men in their investigation, after adjustment for FEV₁ level and smoking. Further, they surmised that very slight degrees of asthma, not sufficient to merit clinical diagnosis, may be relevant to the development of chronic airflow obstruction. None of the bronchitic subjects in our investigation experienced clinical episodes diagnostic of asthma, but ventilatory responses to methacholine and to bronchodilator were varied. Perhaps this does reflect varying degrees of incipient or subclinical asthma, the severity of which is related to increased deterioration of ventilatory function. If so, this was predominantly intrinsic or non-atopic as there was no relationship between skin test reactions and the rate of decline of the FEV₁. Interestingly, a non-atopic increase of IgE occurs in some smokers over 55 years of age.¹³ Whether this immunological change can be related to the increased bronchial lability of the patients studied is uncertain for, although most had been smokers, bronchial lability was unrelated to current smoking.

Although we do not know whether bronchial lability has a causal relationship with deterioration of function, it is clearly an important prognostic indicator. The relationship shown between the number of cigarettes smoked and the rate of decline of the FEV₁ is likely to be causal. It confirms the findings of Fletcher *et al*¹ and Bates,¹⁴ showing that the number of cigarettes being smoked is an important prognostic indicator in chronic bronchitis. This is of increased importance in older persons as the rate of decline of the FEV₁ was shown to increase with age, confirming the findings of Fletcher *et al*.¹

Occupational exposure to dust was found to have a weak relationship with the decline of the FEV₁, but no attempt was made to identify a possible gradient of rate of deterioration with intensity of exposure. This group included subjects exposed to either mineral or organic dusts. Both categories

have been shown previously to be associated with greater symptom prevalence and lower ventilatory capacity than that of controls.^{15,16}

No relationship was found between deterioration of ventilatory function and the occupational grading (socioeconomic group) on entry into the investigation. Many of the subjects, however, had worked in several occupations during their lifetime and their final occupation may not have been entirely representative of their life style.

The lesser rate of decline of the FEV₁ in Queensland than in New South Wales or Victoria is an important geographical difference, if valid. The patients recruited in each State were all middle aged ex-servicemen with chronic bronchitis who had relatively well preserved ventilatory function. Their recruitment followed identical procedures in Queensland and New South Wales and was similar in Victoria. There were two entry periods for Victoria, which made this group a little older than those in the other two States and contributed to a lower FEV₁ and FEV₁/VC%. These and other small differences were lessened after removal of the patients who had withdrawn from follow up. For the patients followed the only significant difference between States was that the patients in Victoria were older than those in New South Wales and Queensland. This did not, however, affect the results as the rate of decline of the FEV₁ in Queensland was less than that in Victoria and New South Wales after adjustment for age.

There was no evidence that the withdrawal of patients influenced the differences between States. Calculated from incomplete data the rate of decline of the FEV₁ of the withdrawn Queensland patients was similar to that of patients from Queensland who were followed and was much less than that of those withdrawn in the other two States. Consequently the State differences in the rate of decline of the FEV₁ in the followed group could not be attributed to the withdrawal of patients. The results are likely to be valid for the type of patient investigated, but further work is needed to show whether this applies to patients with other grades of chronic bronchitis, especially as the rate of decline of the FEV₁ of the patients from Queensland was no greater than for symptomless men including smokers. Fletcher *et al*¹ have described a learning effect in serial studies that may artificially reduce the decline in FEV₁, but if this applied in our study it is likely to have occurred in each State and should not have produced the difference found.

That there is a valid geographic effect receives support from the population mortality rates. Although these depend on prevalence as well as severity, they are at least consistent with the occur-

ence of chronic bronchitis of a lesser severity in Queensland. For the five year period 1971–75 the mortality rate from bronchitis and emphysema (490–492, 8th revision of *International Classification of Diseases*) was 4.30 per 1000 in Queensland, 5.34 in New South Wales, and 5.67 in Victoria for men aged 65 years and older.¹⁷ The lower mortality in Queensland was not due to differences in certification whereby deaths from chronic bronchitis or emphysema were allocated to asthma or pneumonia, as there was also a relative deficiency of deaths from both these conditions in Queensland compared with New South Wales and Victoria. The lower mortality in Queensland and the lesser rate of functional deterioration of the patients investigated in that State are unlikely to be due to differences in the low levels of air pollution between the States.^{18–20} Possibly differences in concentration of industry²¹ or in climate are relevant. Because of the warmer climate houses, workplaces, and other buildings are more open and better ventilated in Queensland than in the other two States (at least until recently). Consequently indoor air pollution, which can be high in closed, poorly ventilated buildings, particularly where there is smoking,²² would have been greater in New South Wales and Victoria than in Queensland and may have contributed to the observed differences in the rate of deterioration of ventilatory function.

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