arthritis. Anecdotal evidence that the children often present in clusters, together with some data in support of a geographical distribution, suggests that this uveitis may be a response to a parasitic, viral, or spirochaetal infection met early in life. A preceding fever in some children and the mixture of lymphocytes and polymorphic cells in the aqueous humour further supports this idea.

We thank Christoffel Blindenmission, West Germany,

Miss M Patel for laboratory analysis, and Miss Suzanne Chawner for secretarial help.

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(Accepted 12 June 1989)

Respiratory symptoms as predictors of 27 year mortality in a representative sample of British adults

Lucy Carpenter, Valerie Beral, David Strachan, Kristie L Ebi-Kryston, Hazel Inskip

Abstract

Objective—To examine associations between reported respiratory symptoms (as elicited by questionnaire) and subsequent mortality.

Design—Prospective cohort study.

Setting—92 General practices in Great Britain.

Participants—A nationally representative sample of 1532 British men and women aged between 40 and 64.

Main outcome measures—Mortality from all causes, cardiovascular disease, lung cancer, and chronic bronchitis.

Results—Subjects were interviewed in 1958 regarding various respiratory symptoms (including cough, phlegm, breathlessness, and wheeze) by using a questionnaire which formed the basis of the Medical Research Council's questionnaire on respiratory symptoms. By the end of 1985, 889 deaths had been reported, including 51 in men due to chronic bronchitis. After adjustment for differences in age and smoking habits death rates from chronic bronchitis in men who reported symptoms were greater than those in men who did not for each of the symptoms examined. The adjusted mortality ratios were 3.4 (95% confidence interval 1.8 to 6.5) for morning cough, 3.7 (2.0 to 6.9) for morning phlegm, 6.4 (3.0 to 13.8) for breathlessness when walking on the level, and 10.5 (4.4 to 24.6) for wheeze most days or nights. Mortality ratios were also significantly raised for four episodic symptoms not usually included in more recent respiratory symptom questionnaires—namely, occasional wheeze (mortality ratio 6.0; 95% confidence interval, 2.4 to 15.1), whether affects chest (5.7; 3.1 to 10.3), breathing difficult in summer (4.9; 2.8 to 8.6), and cold usually goes to chest (3.7; 2.0 to 6.8). The excess mortality associated with these symptoms remained significant after further adjustment for breathlessness or phlegm. Ratios for all cause mortality in men and women were also significantly raised for most respiratory symptoms, death rates being some 20-50% higher in people reporting symptoms after adjustment for age, sex, and smoking. Breathlessness was the only symptom significantly associated with excess mortality from cardiovascular disease (mortality ratio 1.4 (95% confidence interval 1.0 to 1.9) for breathlessness when walking on the level). Ratios were generally around unity and not significant for mortality due to lung cancer.

Conclusions—The results suggest that episodic symptoms, which often do not appear in standard respiratory questionnaires, predict subsequent mortality from chronic obstructive airways disease.

This supports the hypothesis that reversible airflow obstruction may be a precursor of progressive and irreversible decline in ventilatory function.

Introduction

In the 1950s there was concern about the high level of morbidity and mortality from chronic bronchitis in Britain; between 1957 and 1961 the death rate from bronchitis was 108/100 000 in men aged 45-64 in England, Wales, and Scotland, which was about 20 times the rate in Denmark and Norway.¹ Within the United Kingdom pronounced variations in mortality were recorded, higher rates being found in urban areas and the lower social classes.^{2,3} One study undertaken at that time to discover the reason for these variations was a survey of respiratory symptoms in a random sample of men and women attending general medical practices in Britain.⁴ The questionnaire developed for that survey subsequently served as the basis for the Medical Research Council's questionnaire on respiratory symptoms, which is widely used today.⁵ The people who were surveyed in 1958 by using the original questionnaire have been followed up to the end of 1985. We describe the associations between their reported respiratory symptoms and their subsequent death rates.

Subjects and methods

Details of the original survey have been reported.⁴ Briefly, the sample consisted of adult men and women chosen at random from the lists of general practitioners in rural and urban areas of England, Wales, and Scotland. Stratified random samples of one man and one woman in each of the five year age groups 40-44, 45-49, 50-54, 55-59, and 60-64 were drawn from each participating practice. Each practice undertook to interview at least one such sample of 10 subjects. If a sampled subject had died or moved a substitute of the same sex was selected at random from the appropriate age group. Of the 1630 people thus sampled and available for examination at the time of the survey in 1958, 1569 (96%) were interviewed. Data relating to 442 wives of sampled men, which were presented in the original report, are not included here because they did not form a representative sample of women in the population.

The questionnaire used in the survey subsequently served as the prototype for the Medical Research Council's questionnaire on respiratory symptoms, though it underwent some revisions in 1966, 1976, and 1986.^{5,6} During this process some of the original

Department of
Epidemiology and
Population Sciences,
London School of Hygiene
and Tropical Medicine,
University of London,
London WC1E 7HT
Lucy Carpenter, MSC,
lecturer
David Strachan, MRCP,
lecturer

Imperial Cancer Research
Fund, Cancer
Epidemiology and Clinical
Trials Unit, University of
Oxford, Gibson Building,
Radcliffe Infirmary, Oxford
OX2 6HE
Valerie Beral, MRCP, director

Department of
Environmental and
Preventive Medicine, St
Bartholomew's Hospital,
Medical College, London
EC1M 6BQ
Kristie L Ebi-Kryston, PHD,
statistician

Medical Research Council
Laboratories, Fajara, Near
Banjul, The Gambia, West
Africa
Hazel Inskip, PHD,
statistician

Correspondence to: Ms
Carpenter.

Br Med J 1989;299:357-61

questions were omitted, others were modified, and a few were retained essentially unchanged. For example, the questions on cough and phlegm in winter (see appendix) bear a close relation to those in the 1976 and 1986 questionnaires. The original questionnaire provided for five categories of severity of breathlessness, two more than commonly used today (appendix). The additional questions were, Do you have to stop for breath after walking about 100 yards [90 m] (or after a few minutes) on the level? and Are you too breathless to leave the house or breathless on undressing? Wheeze was also more finely categorised (into three grades) than in more recent questionnaires—namely, as wheeze with colds only, occasional wheeze, and wheeze most days or nights.

Because of their relevance to studies using later versions of the questionnaire the questions on cough, phlegm, breathlessness, and wheeze listed in the appendix form the core group of symptoms for analysis in this report. Analyses of data relating to three additional questions on symptoms which were not included in subsequent questionnaires are also reported. These were, Does the weather affect your chest? Is your breathing different in summer and winter? and If you get a cold does it usually go to your chest?

In the original report a "standard diagnosis" of bronchitis was defined as a combination of morning phlegm in winter, bouts of cough and phlegm lasting three weeks each winter, and breathlessness when walking on the level (breathlessness category II or higher).⁴ People who reported all of these symptoms were identified to assess the ability of this definition of bronchitis to predict subsequent mortality.

In addition to respiratory symptoms, data were obtained at interview on social class (registrar general's classification⁷) and smoking habits. Subjects were categorised as non-smokers, ex-smokers, or current smokers. For ex-smokers the age at starting and

stopping regular cigarette smoking was recorded, and for current smokers the age at starting smoking and number of cigarettes smoked daily were recorded.

Identifying data on all subjects interviewed were subsequently sent to the NHS's central register at Southport, and for each death notified a copy of the death certificate was obtained. Person years at risk were computed from the date of interview to the end of 1985 or, if death had occurred, to the date of death. The underlying cause of death was coded by using the 8th revision of the International Classification of Diseases. Deaths from all causes (ICD codes 000-999) and from chronic bronchitis (including emphysema) (ICD 490-492, 519), cardiovascular disease (ICD 400-453), and lung cancer (ICD 162) were investigated.

The mortality among subjects reporting a particular symptom (or combination of symptoms) was compared with that among subjects not reporting that symptom and expressed as a mortality ratio; a ratio of 1.0 implied no difference in mortality between the two groups. Death rates were estimated by using deaths and person years at risk observed in the cohort during the 27 years of follow up. For most of the analyses deaths and person years at risk were cross classified according to age at interview (five groups: 40-44, 45-49, 50-54, 55-59, 60-64), sex, smoking state (non-smoker, ex-smoker, current smoker), and response to each question on symptoms. Mortality ratios adjusted for age, sex, and smoking were estimated from these data by the method of maximum likelihood using the generalised linear interactive modelling (GLIM) computer package⁸ as described by Breslow and Day.⁹

In further analyses of mortality from chronic bronchitis mortality ratios were estimated separately for three follow up periods—namely 0-4, 5-9, and 10 or more years after the date of interview. Additional adjustment for social class (as groups I, II, III, IV, and V) was performed in some analyses, and two alternative classifications of smoking habit were also examined—namely, current amount smoked (five groups: non-smokers, ex-smokers, current smokers of 0-9, 10-19, or 20 or more cigarettes a day) and years of smoking (five groups: non-smokers, ex-smokers who had smoked for less than 30 years or 30 years or more, and current smokers who had smoked for less than 30 years or 30 years or more).

Thirty subjects who had either emigrated or could not be traced at the NHS's central register were excluded from the analyses. One woman was excluded because she had a permanent tracheostomy tube. A further five men and one woman were excluded because their dates of birth were not known. This report therefore relates to 1532 subjects (768 men, 764 women)—that is, 98% of the original sample interviewed. Fourteen men and 21 women who were disabled at the time of interview were excluded from analyses of questions on breathlessness.

Results

Table I gives the prevalence at interview of the symptoms analysed. Response rates for the different questions were high. Wheeze and morning cough were the most commonly reported symptoms in men, with prevalences of 49% and 47% respectively. The prevalence of cough and phlegm was substantially lower in women than men but there was less difference in the prevalence of other symptoms. Breathlessness and wheeze were the commonest of the core group of respiratory symptoms in women, with prevalences of 42% and 36% respectively. "Cold usually goes to chest" was the additional respiratory symptom most commonly reported, the prevalence being about 40% in men and women. Smoking was particularly common in men, three quarters of whom were current smokers.

TABLE 1—Percentage prevalence of symptoms in men and women distributed by age and smoking report at interview. Total number responding to each question given in parentheses

Symptom	Sex	Age at interview		Smoking report			Total
		<55	≥55	Non-smoker	Ex-smoker	Current smoker	
Morning cough	M	43	53	13	27	55	47 (765)
	F	20	22	12	22	36	21 (760)
Day or night cough	M	16	24	8	14	23	20 (759)
	F	9	15	8	10	19	12 (756)
Morning phlegm	M	34	49	9	28	47	41 (762)
	F	15	21	10	21	31	18 (758)
Day phlegm	M	13	21	2	13	18	16 (762)
	F	5	10	4	9	11	7 (757)
Bouts of cough and phlegm	M	20	32	13	24	26	25 (768)
	F	16	18	11	16	28	17 (763)
Breathlessness*†:							
Category I	M	20	22	12	20	22	21 (754)
	F	25	30	27	23	28	27 (743)
Category II	M	6	16	6	10	11	11 (754)
	F	7	14	11	12	9	10 (743)
Category III, IV or V	M	2	9	0	8	5	5 (754)
	F	3	6	4	5	4	5 (743)
Wheeze†:							
Category I	M	25	26	19	23	27	25 (768)
	F	25	27	21	32	31	26 (764)
Category II	M	11	14	11	13	13	13 (768)
	F	5	7	6	0	7	6 (764)
Category III	M	8	15	2	10	12	11 (768)
	F	4	4	3	6	5	4 (764)
Weather affects chest	M	22	39	17	32	30	30 (768)
	F	16	26	16	31	24	20 (764)
Breathing different in summer	M	14	26	10	19	20	19 (753)
	F	9	15	9	20	13	11 (743)
Cold usually goes to chest	M	38	47	23	42	44	42 (768)
	F	36	44	31	51	52	40 (764)
Standard diagnosis of bronchitis*	M	4	17	2	10	10	10 (753)
	F	2	5	3	8	3	4 (743)
Total	M	55	45	7	18	75	100 (768)
	F	55	45	57	9	35	100 (764)

*Fourteen men and 21 women who were disabled were excluded from analyses of questions concerning breathlessness.

†Categories of breathlessness and wheeze are defined in the appendix.

TABLE II—Rate ratios in respect of mortality from all causes, cardiovascular disease, lung cancer, and chronic bronchitis according to symptom report at interview. Values adjusted for age, sex, and smoking (95% confidence intervals in parentheses)

Symptom	All causes (ICD* codes 000-999)			Cardiovascular disease† (ICD* codes 400-453)	Lung cancer† (ICD* code 162)	Chronic bronchitis‡ (ICD* codes 490-492, 519)
	Men	Women	Both sexes			
Morning cough	1.4 (1.2 to 1.7)	1.1 (0.9 to 1.4)	1.3 (1.1 to 1.5)	1.0 (0.8 to 1.3)	1.6 (1.0 to 2.6)	3.4 (1.8 to 6.5)
Day or night cough	1.4 (1.1 to 1.7)	1.2 (0.9 to 1.6)	1.3 (1.1 to 1.6)	1.1 (0.8 to 1.4)	1.9 (1.1 to 3.2)	4.2 (2.4 to 7.4)
Morning phlegm	1.4 (1.2 to 1.7)	1.2 (0.9 to 1.6)	1.3 (1.2 to 1.6)	1.1 (0.9 to 1.4)	1.3 (0.8 to 2.2)	3.7 (2.0 to 6.9)
Day phlegm	1.4 (1.2 to 1.8)	1.1 (0.8 to 1.6)	1.4 (1.1 to 1.6)	1.2 (0.9 to 1.6)	1.4 (0.7 to 2.6)	5.0 (2.9 to 8.7)
Bouts of cough and phlegm	1.3 (1.1 to 1.6)	1.1 (0.8 to 1.4)	1.2 (1.1 to 1.4)	1.1 (0.9 to 1.4)	1.1 (0.6 to 1.9)	4.0 (2.3 to 7.1)
Breathlessness‡:						
Category I	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.4)	1.1 (0.9 to 1.3)	0.9 (0.7 to 1.2)	1.2 (0.7 to 2.2)	1.9 (0.8 to 4.3)
Category II	1.5 (1.2 to 2.0)	1.5 (1.1 to 2.1)	1.5 (1.2 to 1.9)	1.4 (1.0 to 1.9)	0.9 (0.3 to 2.2)	6.4 (3.0 to 13.8)
Category III	1.9 (1.1 to 3.3)	1.4 (0.7 to 2.6)	1.7 (1.1 to 2.5)	1.6 (0.9 to 2.9)	1.0 (0.1 to 7.4)	6.8 (1.9 to 24.4)
Category IV	1.8 (0.9 to 3.6)	2.2 (1.1 to 4.3)	2.0 (1.2 to 3.2)	2.0 (1.1 to 5.2)	1.9 (0.3 to 13.8)	13.2 (3.7 to 47.6)
Category V	3.3 (1.9 to 5.8)	8.1 (1.9 to 34.7)	3.6 (2.1 to 6.0)	2.9 (1.3 to 6.5)	0.1 (0.0 to 117.5)	37.4 (14.5 to 96.5)
Wheeze:						
Category I	1.1 (0.9 to 1.4)	1.2 (1.0 to 1.5)	1.2 (1.0 to 1.4)	1.0 (0.8 to 1.3)	1.4 (0.8 to 2.4)	3.6 (1.5 to 8.5)
Category II	1.3 (1.0 to 1.7)	0.7 (0.4 to 1.2)	1.1 (0.9 to 1.4)	1.0 (0.7 to 1.4)	0.7 (0.3 to 1.9)	6.0 (2.4 to 15.1)
Category III	1.5 (1.1 to 1.9)	1.7 (1.1 to 2.6)	1.5 (1.2 to 1.9)	1.3 (0.9 to 1.8)	0.7 (0.2 to 1.9)	10.5 (4.4 to 24.6)
Weather affects chest	1.4 (1.2 to 1.7)	1.3 (1.0 to 1.6)	1.3 (1.2 to 1.6)	1.0 (0.8 to 1.2)	1.2 (0.7 to 2.0)	5.7 (3.1 to 10.3)
Breathing different in summer	1.5 (1.2 to 1.8)	1.2 (0.9 to 1.6)	1.4 (1.2 to 1.7)	1.3 (1.0 to 1.7)	1.5 (0.9 to 2.7)	4.9 (2.8 to 8.6)
Cold usually goes to chest	1.2 (1.0 to 1.5)	1.1 (0.9 to 1.3)	1.2 (1.0 to 1.3)	1.0 (0.8 to 1.2)	0.9 (0.5 to 1.4)	3.7 (2.0 to 6.8)
Standard diagnosis of bronchitis‡	1.8 (1.4 to 2.4)	1.2 (0.7 to 2.0)	1.6 (1.3 to 2.1)	1.5 (1.1 to 2.1)	0.9 (0.3 to 2.4)	9.5 (5.3 to 16.9)

*International Classification of Diseases, 8th revision.

†Both sexes except in case of bronchitis, for which analyses are confined to men.

‡Fourteen men and 21 women who were disabled were excluded from analyses of questions concerning breathlessness.

In general, symptoms increased in prevalence with age and smoking.

Eight hundred and eighty nine deaths (521 in men, 368 in women) were reported to have occurred before the end of 1985. Of these, over half were attributed to either chronic bronchitis (51 men, five women), cardiovascular disease (245 men, 189 women), or lung cancer (53 men, 15 women). The fifty six deaths from chronic bronchitis accounted for roughly half of all 117 deaths certified as due to respiratory disease. Of the remainder, 54 were due to influenza or pneumonia (ICD codes 480-486), two to asthma (ICD 493), and five to other respiratory diseases.

MORTALITY FROM ALL CAUSES, CARDIOVASCULAR DISEASE, AND LUNG CANCER

Table II shows the age, sex, and smoking adjusted mortality ratios associated with each symptom in respect of deaths from all causes, chronic bronchitis, cardiovascular disease, and lung cancer. For all causes of death mortality ratios for both sexes were generally significant and tended to lie between 1.2 and 1.5. Ratios for breathlessness were highest and increased with severity of the symptom. Apart from breathlessness and wheeze, ratios tended to be lower and not significant among women as compared with men.

Ratios for mortality from cardiovascular disease (men and women) were highest for breathlessness and increased with the severity of breathlessness. Mortality ratios for all other symptoms were around unity and not significant except for the standard diagnosis of chronic bronchitis, which included breathlessness. For lung cancer mortality ratios were highest for both questions on cough, but only for day or night cough did the confidence interval not include unity.

MORTALITY FROM CHRONIC BRONCHITIS

Only five deaths from bronchitis were certified in women, and analyses of mortality from chronic bronchitis were therefore confined to men. Of the 51 men who died of chronic bronchitis, 22 (43%) had reported symptoms that met the criteria for a standard diagnosis of bronchitis and 10 reported none of these symptoms. Of the 52 men who met the criteria for a standard diagnosis but did not die of chronic bronchitis, two died of lung cancer, 29 died of cardiovascular disease, and 14 died of other causes. Ratios for mortality from chronic bronchitis in men were significantly raised for every symptom examined and were highest among those reporting moderate or severe breathlessness (category II or higher), persistent

wheeze (category III), and those fulfilling the criteria for a standard diagnosis of bronchitis. Mortality ratios were also significantly raised for each of the additional symptoms examined, particularly "weather affects chest" and "breathing different in summer." Ratios for cough and phlegm were generally lower and in each case were slightly lower among men who experienced the symptom in the morning compared with during the day or night.

Fourteen deaths from chronic bronchitis in men occurred in the first five years, nine between five and 10 years, and 28 more than 10 years after the date of interview. Eleven of the 14 deaths in the first five years occurred in men who met the criteria for a standard diagnosis, and the mortality ratio was particularly high (31.0; 95% confidence interval, 8.4 to 114.5). Mortality ratios during this period were also high for day or night cough (14.7; 4.1 to 53.0), day phlegm (18.0; 5.0 to 65.0), and wheeze (category III; 26.4, 3.2 to 218.1). Ratios could not be estimated for breathlessness during this period because there were no deaths among non-breathless men. During the second five years of follow up mortality ratios were generally much lower. At 10 or more years after the initial symptom report, however, all symptoms examined continued to be associated with excess mortality from chronic bronchitis. Mortality ratios during this period were highest for persistent wheeze (category III; mortality ratio 4.9, 1.6 to 14.9), breathlessness (category II; 3.8, 1.4 to 10.6), and "weather affects chest" (3.8, 1.8 to 8.0). As in analyses of data for the whole follow up period (table II), mortality ratios for wheeze and breathlessness increased with the severity of symptoms during this period of follow up.

As three quarters of the men who were interviewed were smokers, it was important to examine the effect of adjusting for smoking as measured by amount smoked or number of years of smoking as opposed to the three categories of smoking (non-, ex-, current) used above. When mortality from chronic bronchitis in men was analysed after adjustment for either amount smoked daily or number of years of smoking mortality ratio estimates as presented in table II changed very little (not shown). Adjustment for social class in addition to age and smoking tended to diminish mortality ratios for bronchitis, but only slightly. For example, the mortality ratio for category II breathlessness was 5.7 (95% confidence interval, 2.6 to 12.5).

Mortality ratios for chronic bronchitis were also adjusted for phlegm (defined as report of either morning or day phlegm) or breathlessness, or both, to

TABLE III—Rate ratios in respect of mortality from chronic bronchitis (ICD (8th revision) codes 490, 492, 519) in men* according to symptom report at interview and after adjustment for various factors (95% confidence intervals in parentheses)

Symptom	Adjusted for age and smoking	Adjusted for age, smoking, and breathlessness	Adjusted for age, smoking, and phlegm†	Adjusted for age, smoking, phlegm,† and breathlessness
Morning cough	3.4 (1.8 to 6.4)	1.5 (0.7 to 3.1)	2.1 (0.9 to 4.7)	1.1 (0.5 to 2.7)
Day or night cough	4.2 (2.4 to 7.4)	1.8 (0.9 to 3.5)	2.9 (1.6 to 5.6)	1.6 (0.8 to 3.1)
Morning phlegm	3.6 (2.0 to 6.8)	2.0 (1.0 to 3.9)	—	—
Day phlegm	5.0 (2.9 to 8.7)	2.7 (1.4 to 5.0)	—	—
Bouts of cough and phlegm	4.0 (2.3 to 6.9)	1.9 (1.0 to 3.7)	2.8 (1.5 to 5.4)	1.7 (0.9 to 3.5)
Breathlessness:				
Category I	1.9 (0.8 to 4.3)	—	1.6 (0.7 to 3.7)	—
Category II	6.5 (3.1 to 14.0)	—	5.1 (2.2 to 11.5)	—
Categories III-IV	15.7 (7.2 to 34.2)	—	12.0 (5.2 to 27.8)	—
Wheeze:				
Categories I and II	4.3 (1.9 to 9.5)	2.9 (1.2 to 6.7)	3.6 (1.5 to 8.2)	2.6 (1.1 to 6.3)
Category III	10.5 (4.5 to 24.8)	3.5 (1.3 to 9.6)	7.6 (3.0 to 19.6)	3.1 (1.1 to 8.8)
Weather affects chest	5.6 (3.1 to 10.2)	2.8 (1.4 to 5.9)	4.4 (2.3 to 8.4)	2.6 (1.2 to 5.5)
Breathing different in summer	4.8 (2.7 to 8.4)	2.0 (1.0 to 4.0)	3.5 (1.9 to 6.4)	1.9 (0.9 to 3.7)
Cold usually goes to chest	3.6 (1.9 to 6.7)	2.2 (1.2 to 4.3)	2.7 (1.4 to 5.2)	2.1 (1.0 to 4.1)

*Fourteen men who were disabled were excluded from all analyses of all questions.

†Phlegm assessed as report of either morning phlegm or day phlegm versus report of neither.

assess the additional contribution made by other symptoms in predicting mortality (table III). Adjustment for phlegm or breathlessness (by using categories I, II, and III-V) reduced mortality ratios for all symptoms, the reductions being slightly greater after adjustment for breathlessness. When adjustment was made for both phlegm and breathlessness mortality ratios for cough and bouts of cough and phlegm were no longer raised significantly, whereas those for wheeze and "weather affects chest" remained significantly above unity. When adjustment was made for breathlessness and wheeze mortality ratios for morning phlegm and day phlegm were 1.6 (95% confidence interval, 0.8 to 3.2) and 2.3 (1.2 to 4.4) respectively.

Finally, analyses were performed restricting data to men who had reported no breathlessness at interview. Mortality ratios for chronic bronchitis for each of the symptoms were generally lower and not significant in this subgroup. Only that for occasional wheeze (category II) was raised significantly (mortality ratio 3.7; 95% confidence interval, 1.2 to 11.6).

Discussion

The general practitioners who took part in this survey consisted of 92 members of the (then) College of General Practitioners who agreed to participate.⁴ Though the resulting sample of subjects was therefore not strictly random, marital state and social class distributions were very similar to those of people in the same age groups in England and Wales in 1951⁴ and 1961.^{10,11} Sex specific prevalences of smoking in this sample were also in line with published data for the age group and period examined.¹² Certainly in these respects the sample seemed to be representative of the general population at that time.

Follow up was performed by using the routine system for reporting mortality in the United Kingdom and, though possibly some deaths may have been missed, mortality ratios would be biased only if, for example, deaths in people with symptoms were more likely to be reported to the NHS's central register. This type of bias, however, is perhaps less relevant when assessing the relative importance of different respiratory symptoms as predictors of mortality.

MORTALITY FROM ALL CAUSES, CARDIOVASCULAR DISEASE, AND LUNG CANCER

The association of mortality from all causes and cardiovascular disease and a report of breathlessness found in our series is consistent with other studies. Ferris *et al* found excess mortality from all causes to be associated with breathlessness in men and women.¹³

Though many of the respiratory symptoms that we examined seemed less predictive of subsequent all cause mortality in women than men, reported breathlessness and wheeze were more alike in their ability to predict all cause mortality in the two sexes. Higgins and Keller found breathlessness to be the symptom with highest predictive power for four year mortality in Tecumseh, particularly from coronary heart disease.¹⁴ More recently breathlessness, but not production of phlegm, was consistently associated with mortality from cardiovascular disease independently of several other coronary risk factors in data from four prospective studies of men.¹⁵ In another study breathlessness was independently associated with an increased risk of a major ischaemic heart disease event in men with no evidence of pre-existing cardiac disease.¹⁶ Breathlessness on exertion may be symptomatic of either cardiac or respiratory disease. Spirometric evidence of airways obstruction is an important predictor of mortality from all causes and cardiovascular disease independently of age, smoking behaviour, and coronary risk factors.^{17,18} Among Whitehall civil servants, however, adjustment for forced expiratory volume in one second (percentage predicted) reduced the effect of breathlessness on all cause and cardiovascular mortality by only a small amount,¹⁸ suggesting that much of the ability of this symptom to predict subsequent mortality is due to its relation with cardiac rather than respiratory disease.

Several other studies have found associations between lung cancer and production of phlegm even after adjustment for smoking.^{19,21} The mortality ratios that we found had wide confidence intervals and, though not significantly different from unity, were consistent with these earlier reports.

MORTALITY FROM CHRONIC BRONCHITIS

Mortality ratios for bronchitis in men were significantly raised for every symptom examined (table II), even after 10 or more years of follow up. As for all causes, breathlessness emerged as the most powerful predictor. The importance of airways obstruction as distinct from mucus hypersecretion in determining subsequent mortality from chronic respiratory disease is now well recognised.²⁰ Among Whitehall civil servants much of the effect of breathlessness on 15 year mortality from chronic bronchitis was accounted for by its association with a reduction in forced expiratory volume in one second.²²

This study is of particular interest because it included episodic symptoms which were subsequently omitted from the Medical Research Council's questionnaire (occasional wheeze, chesty colds, seasonal variation in breathing, weather affecting chest). These seemed to be significant predictors of mortality from bronchitis even after adjustment for breathlessness. Their weak association with mortality from lung cancer suggests that their relation with death from bronchitis is unlikely to be explained by inadequate adjustment for smoking. These four complaints may be early symptoms of the progressive and irreversible decline in ventilatory function that is the hallmark of fatal and disabling non-specific lung disease. Alternatively they may indicate episodes of reversible airways obstruction which would normally be considered characteristic of bronchial asthma.^{24,25} If this is the case then their association with subsequent mortality attributed to chronic bronchitis or emphysema suggests a link between reversible and irreversible airways obstruction.

Nearly 30 years ago Dutch workers suggested that individual characteristics related to asthma, such as an allergic constitution and non-specific bronchial hyperreactivity, were important in determining which smokers subsequently developed irreversible airways obstruction.^{26,27} Follow up studies of middle aged

men have found a poor correlation between atopic manifestations and decline in ventilatory function,^{28 29} but in two cohorts increased bronchial reactivity to inhaled histamine²⁹ or methacholine³⁰ has been associated with a faster rate of decline in forced expiratory volume in one second. Interpretation of these last findings is difficult because bronchial hyperresponsiveness may be a consequence rather than a cause of narrowing of the airways.³¹ A longitudinal study of adults diagnosed with asthma and matched controls, however, found a ninefold increase in subsequent risk of death from chronic respiratory disease (excluding asthma) among those with asthma.³² Though misdiagnosis may partly explain this increase, it is consistent with our findings and with evidence from longitudinal²⁸ and cross sectional³³ studies which suggest that asthmatic patients are particularly susceptible to rapid decline in ventilatory function and the development of irreversible airways obstruction.

Conclusion

The standard diagnosis of bronchitis adopted in the College of General Practitioners' study reflected the thinking of that time in considering production of phlegm and exertional breathlessness to be symptoms of the same disease. This is no longer thought to be appropriate.³⁴ By including breathlessness in their diagnostic criteria the investigators ensured that their "standard diagnosis" was predictive of subsequent death from bronchitis. Subsequently the definition of chronic bronchitis focused on productive cough, indicating hypersecretion of mucus.³⁵ The development of the widely used Medical Research Council's questionnaire⁵ may have had the unfortunate consequence that other respiratory symptoms of an episodic nature have been excluded from many subsequent investigations. Our findings suggest that these may deserve greater attention in the future.

This work was supported by the Medical Research Council. We thank Betty Killick for coding the data, Noreen Maconochie and Jayne Hartnell for help with computing, Evelyn Middleton and Nina Saroi for typing the manuscript, and Hugh Markowe for helpful comments on the text.

Appendix

Questions on cough, phlegm, breathlessness, and wheeze as worded in original College of General Practitioners' questionnaire on respiratory symptoms.

MORNING COUGH

Do you cough at all on getting up or first thing in the morning in winter?

DAY OR NIGHT COUGH

Do you go on coughing during the day or at night in winter?

MORNING PHLEGM

Do you bring up any phlegm at all on getting up or first thing in the morning in winter?

DAY PHLEGM

Do you go on bringing up phlegm during the day in winter?

BOUNTS OF COUGH AND PHLEGM

Do you get bouts of cough and phlegm lasting for at least three weeks each winter?

BREATHLESSNESS

- (I) Are you troubled by shortness of breath? (If no, check: Not even on hurrying on the level or walking up a slight hill?)
- (II) Do you have to walk slower than other people of your own age on the level because of breathlessness?
- (III) Do you ever have to stop for breath when walking at your own pace on the level?

- (IV) Do you have to stop for breath after walking about 100 yards [90 m] (or after a few minutes) on the level?
- (V) Are you too breathless to leave the house or breathless on undressing?

WHEEZE

Does your chest ever sound wheezy or whistling?

- (I) Only with colds.
- (II) Occasionally (apart from colds).
- (III) Most days or nights.

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(Accepted 31 May 1989)