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Philip Ellman Lecture

Some Recent Advances in the Prevention and Treatment of Chronic Bronchitis and Related Disorders

With Special Reference to the Effects of Cigarette Smoking

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It is four years since Philip Ellman died at the height of his career, yet the vigour of his life and work was such that memory has to exert no effort to bridge the gap of time. His enthusiasm, his friendliness, his intense preoccupation with the whole of life, professional and personal, remain alive in our memories.

It was this vigour and enthusiasm of Philip Ellman that most distinguished him from his more pedestrian contemporaries. There are few men today who, with all the distractions of a busy practice, can make original, scholarly contributions in more than one field of medicine. His bibliography, extending over a period of thirty years, contains nearly a hundred contributions to medical literature. Many of these were case reports, for Philip Ellman was a keen participant in medical meetings of all kinds and he was perhaps never so happy as when debating clinical problems, for he was fascinated by the rare and unusual. But he also contributed steadily to the advance of clinical knowledge, making original observations in many fields of medicine. His deep interest lay in rheumatic diseases, in chest diseases and in the relationship between the two: it is appropriate that this interest should be reflected in the regulations for his memorial lectures which are to be given on 'some aspect of the prevention and curative treatment of diseases of the chest or rheumatic diseases'.

I have decided to devote this lecture to my special interest of chronic bronchitis and emphysema. A recent follow-up of patients attending my clinic has shown a fairly uniform progression of their disability despite all the resources of modern treatment. I think this is the experience of most chest physicians today and this should lead us to devote more energy to prevention. For effective prevention we must understand ætiology and so I shall devote most of my lecture to describing what we have learnt, mostly from epidemiological studies, about the ætiology and natural history of chronic bronchitis. I shall have only some general comments to make about treatment.

Bronchitis Mortality

The epidemiologist first looks to mortality data for indications of ætiology. Since the Registrar General does not record *smoking habits* his figures provide no direct evidence on the effects of smoking on bronchitis mortality, and the rapidly rising male lung cancer mortality in the past 30 years might suggest that increasing cigarette consumption among men had not affected bronchitis mortality. But mortality among women, with many fewer cigarette smokers in the older age groups, has declined over this period, partly owing to chemotherapy and other improved methods of treatment. Thus the constant male mortality represents a balance between an increase attributable to cigarette smoking and a decline attributable to therapy (Fletcher 1965). The consequent changes in the male/female bronchitis mortality ratio for bronchitis have been similar to those for lung cancer although in the case of cancer the increase has been steeper (Table 1). Both are compatible with the earlier adoption of cigarette smoking by men. Direct evidence about the effect of smoking is provided by Doll & Hill's study (1964) of the mortality of British doctors which shows a steady increase of bronchitis mortality with increasing cigarette consumption and a lower rate in ex-smokers and pipe smokers. Confirmatory, less direct, evidence has been provided by Wicken & Buck (1964) and by Dean (1965).

Table 1
Male/female mortality ratios for bronchitis and lung cancer in England and Wales 1916–60. Subjects aged 45–64

Period	*Lung cancer*	*Bronchitis*
1916–20	1·7	1·23
1921–25	2·1	1·22
1926–30	2·7	1·41
1931–35	3·6	1·80
1936–40	4·4	2·46
1941–45	5·4	3·28
1946–50	6·6	3·90
1951–55	7·5	4·35
1956–60	7·6	4·20

An association between indices of *air pollution* and bronchitis mortality has repeatedly been demonstrated and there is ample evidence of the mortal effect of acute episodes of smog upon bronchitic patients. Evidence that the association is causal has been reviewed elsewhere (Fletcher 1962, Reid 1964). There is little evidence from mortality figures to indicate that *occupation* has an important influence on bronchitis mortality (Fletcher 1958).

Two of the most striking features of bronchitis mortality remain largely unexplained. First, in this country mortality is five times greater in unskilled labourers and their wives than in the professional classes. This gradient has persisted despite the great access of welfare in lower social classes. Some of it may be due to air pollution, since unskilled labourers live in the more polluted parts of our towns, and some may be due to migration down the social gradient owing to the effects of the disease itself (Meadows 1961). There is no evidence that it is due to overcrowding (Fairbairn & Reid 1958, Buck & Brown 1964). The second feature is the exceedingly high mortality rate in the British Isles compared with any other country in the world. Part but not all of the British excess may be due to differences in habits of certification of causes of death. The excess is often attributed to air pollution but since the death rate in our 'truly rural' areas is still some 20 times greater than the rate in Scandinavian countries or the USA there must be other factors. Both these features indicate that the greater part of bronchitis mortality must be preventable and this fact presents a great challenge.

The Chronic Bronchitis Syndrome

Chronic bronchitis comprises a complex of disordered functions which are combined with emphysema as a single disease in mortality statistics. To elucidate the ways in which ætiological factors act we have to consider the components of the complex separately. I shall follow the classification of chronic bronchitis which was recently advanced by the Medical Research Council's Committee on the Ætiology of Chronic Bronchitis (1965) and which is shown in Table 2. This is a logical classification and may be related to the natural history of the disease.

Table 2
Classification of chronic bronchitis

Simple chronic bronchitis 'Chronic or recurrent increase in the volume of mucoid bronchial secretion sufficient to cause expectoration'
Mucopurulent chronic bronchitis 'Chronic bronchitis in which the sputum is persistently or intermittently purulent when this is not due to localized bronchopulmonary disease'
Chronic obstructive bronchitis 'Chronic bronchitis with persistent widespread narrowing of the bronchial airways, at least on expiration, causing increased resistance to airflow'

Ætiology of Simple Bronchitis

Hypersecretion of bronchial mucus which constitutes simple chronic bronchitis must be regarded as the primary abnormality in this disease, for we cannot say that bronchitis exists in its absence. By itself, however, it is not a disabling condition. There are many people who expectorate small quantities of sputum for many years without developing any more advanced respiratory disorder.

The study of simple chronic bronchitis has been facilitated in recent years by standardized diagnostic techniques for epidemiological and clinical use which were pioneered in this country and have now received wide international acceptance. Standardized questions about respiratory symptoms (Medical Research Council 1960) permit comparisons to be made between the results of clinical and field surveys by reducing the bias of the interviewer, the importance of which was first shown by Cochrane *et al.* (1951). The questionnaires have been translated into many foreign languages permitting international comparisons (Olsen & Gilson 1960, Mork 1962, Huhti 1965) but questions still remain an inaccurate diagnostic tool and the simple technique of collecting and measuring sputum volume (Elmes *et al.* 1959) has the merit of greater objectivity and greater validity in relation to bronchial hypersecretion (Fletcher 1964*a*). The pathological basis of simple bronchitis has been shown to be hypertrophy of the mucus-secreting glands and goblet cells lining the bronchi. Indices have been proposed for its quantitative assessment (Reid 1960*a*, Restrepo & Heard 1963).

Both epidemiological and pathological studies have identified three main factors responsible for the development of chronic simple bronchitis.

(1) *Cigarette smoking* has been shown to be quantitatively related to the prevalence of simple chronic bronchitis while pipe smokers and ex-smokers have a much lower prevalence (Higgins 1959, Fletcher & Tinker 1961, Holland & Reid 1965) and mucous gland hypertrophy has been shown to be more marked in cigarette smokers than in non-smokers, pipe smokers or cigar smokers (Auerbach *et al.* 1962, Thurlbeck *et al.* 1963).

(2) *Air pollution* appears to play a part at least in the more severe grades of simple chronic bronchitis – expectoration of phlegm throughout the day – for this symptom is more prevalent in men in England than in those smoking similar amounts in Norway or in North America (Mork 1962, Holland *et al.* 1965) and the same contrast has been shown between men working in London and those in rural areas in England (Holland 1964).

(3) *Acute bronchial infection* is associated with a temporary increase of mucous secretion and there is some evidence that this may develop into simple chronic bronchitis. Even in rural areas some 5–10% of non-smokers have a productive cough which cannot be attributed to smoking or air pollution (Higgins & Cochran 1958, Holland 1964, Holland & Reid 1965) but little attention has been paid to the ætiology of this expectoration. We have recently looked into this question in a group of working men in London on whom we are conducting a prospective survey. We have 131 non-smokers of whom 29 (22%) have regularly produced sputum specimens every six months over the past four years. Nearly 50% of the cigarette smokers regularly produce sputum. We asked all the non-smokers and a control group of cigarette smokers of similar age who produced similar sputum volumes about their early medical history (Table 3). The only significant difference was an increased frequency of childhood bronchitis in the non-smokers. This suggests that childhood respiratory tract infections may initiate persistent bronchial hypersecretion in some subjects who may be less likely to take up cigarette smoking than their more fortunate fellows. Since the non-smokers without sputum and smokers with sputum are so similar in respect of childhood medical history, smoking rather than early illness appears to be the major ætiological factor responsible for the increased frequency of simple bronchitis among the smokers.

Since the mucoid sputum of simple bronchitis frequently harbours pathogenic bacteria (Miller & Jones 1964) and bronchoscopic studies (Laurenzi *et al.* 1961, Lees & McNaught 1959) have shown that in such cases the bronchi have often lost their normal sterility and harbour a bacterial flora like that of the upper respiratory tract, it is usually concluded that the normal defences of the lower respiratory tract against bacterial colonization are impaired by mucus hypersecretion. It is, however, possible that this persistent infection may not only initiate but also play a part in maintaining hypersecretion. Reid's (1960*b*) report that mucous gland hypertrophy in cases of bronchiectasis is confined to affected lobes provides further evidence that infection may initiate chronic hypersecretion.

Table 3

Prevalence of illness before the age of 15 in a group of adult non-smokers with and without sputum and a group of smokers matched for age and sputum volume

	Non-smokers				*Smokers*	
	With sputum (29 men)		*Without sputum (92 men)*		*With sputum (92 men)*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Catarrh	2	6·9	5	5·4	16	17·4
Discharging ears	5	17·2	8	8·7	9	9·8
Bronchitis	8	27·6●	6	6·5	7	7·6
Asthma	2	6·9	0	0	1	1·1
Hay fever	1	3·4	4	4·3	6	6·5
Pneumonia	3	10·3	10	10·9	13	14·1
Whooping-cough	9	31·0	32	34·8	35	38·0
Tonsils and adenoids	9	31·0	23	25·0	26	28·3

●Significantly different from other groups

Mucopurulent Chronic Bronchitis

Simple chronic bronchitis is almost entirely a pre-clinical condition; for many men regard their productive cough as a normal bodily function. When active infection arises the sputum becomes purulent and, if the patient suffers malaise, the doctor may be consulted: but many episodes of bronchial infection are never brought to the doctor. Indeed these illnesses often have very little disabling effect until the patient has already got severe obstructive bronchitis. Diagnosis of mucopurulent bronchitis depends upon inspection of the sputum and this must be done properly. We should inspect the sputum of our patients in a suitably sized transparent container and learn to recognize pus reliably (Miller & Jones 1963). Pus cannot be detected reliably in opaque containers or in transparent containers with a layer of sputum deeper than 3 or 4 cm. The ordinary cardboard sputum carton which is so often used in our wards is a great handicap to accurate diagnosis.

In both epidemiological surveys and clinical practice we often obtain a history of recurrent 'chest illnesses' in subjects whom we would otherwise regard as having simple bronchitis. At the time of the interview the sputum may be mucoid but the patient says that the sputum was yellow or thick during the illness he reports. We have found these histories are often unreliable. In a group of 90 men followed at regular intervals throughout one winter we noted that a deterioration of chest symptoms described by the men as an increase in phlegm, wheezing or dyspnœa might be unaccompanied by any change in the volume or colour of sputum or of FEV (Angel *et al.* 1965). This is a clinical problem which needs further study.

Despite this uncertainty there is no doubt that many of the 'chest illnesses' about which we obtain histories are due to exacerbations of bronchial infection. These illnesses occur more frequently in subjects with larger sputum volumes (Fletcher *et al.* 1959, Fletcher & Tinker 1961, Angel *et al.* 1965) and it is widely believed (McLean 1956, Oswald 1964) that this association is one of cause and effect, the excessive mucus encouraging recurrent proliferation of the chief bronchial pathogens – pneumococci and *H. influenzæ* (Reid 1960*b*). Smoking and air pollution also appear to encourage infection independently of simple bronchitis. In 588 men without sputum interviewed by my colleagues at the beginning of our present prospective survey more than twice as many smokers as non-smokers said they had had a bronchitic type of chest illness in the previous three years (Table 4). This effect of smoking was smaller than the effect of hypersecretion, for illnesses were more frequent in the men with sputum than without, whether or not they were smokers.

Table 4

Percentage of men aged 30–59 having had one or more chest illnesses with increased phlegm in past three years (No. of men in brackets)

	No sputum	*<2·5 ml sputum*	*2·5+ ml sputum*
Smokers	16·2 (59)	20·1 (28)	24·3 (71)
Ex-smokers and non-smokers	6·7 (15)	20·9 (9)	26·3 (10)

Smokers versus ex-smokers and non-smokers significant.
No sputum versus sputum significant in both groups.
<2·5 ml versus 2·5+ ml not significant in either group

Holland (1965, personal communication) has confirmed this observation in a survey of post-office workers in England and the USA. More objective evidence of mucopurulent bronchitis can be obtained from sputum specimens. Sputum more often contains pus in London than in rural towns and pus is even less common in the sputum of men of the same age in the USA (Holland *et al.* 1965). Mork (1962) reported a similar contrast between men living in London and in Bergen. It seems that smoking and air pollution may both impair the defences of the lower respiratory tract against the assault of infective agents, viral or bacterial (Laurenzi *et al.* 1963), possibly assisted by impairment of ciliary activity which may be caused by both cigarette smoke (Ballenger 1960) and components of air pollution (Tremer *et al.* 1959).

The role of virus infection is still uncertain. Most investigators have found little evidence of virus infection in exacerbations of bronchitis (Jack & Gandevia 1960, Hennessy 1962, Stark *et al.* 1965). Others (Carilli *et al.* 1964) suggest that this is due to technical inadequacies and that viral infections are frequently responsible for exacerbations.

Chronic Obstructive Bronchitis

Airways obstruction of severity sufficient to cause dyspnœa or to interfere with accustomed activities is what usually brings patients with bronchitis to see their doctors. If, as commonly occurs, the impairment comes on gradually it may be severe before symptoms arise. Fletcher *et al.* (1959) reported a man with a forced expiratory volume (FEV) of only 0·65 litre who was carrying mail-bags around the City of London without any complaint of dyspnœa. Obstructive bronchitis may approach grave levels of impairment without any clinical warning so that treatment is delayed until irreparable damage has been done to the lungs.

Differentiation from Asthma and Emphysema

Here I wish to make a short digression into the difficult problem of the differential diagnosis of the causes of generalized airways obstruction which in conventional clinical terms implies asthma, bronchitis and emphysema. Here we at once encounter the problem of definition. I have already defined chronic obstructive bronchitis. Asthma has been defined as 'widespread narrowing of the bronchial airways with changes of severity over short periods of time either spontaneously or under treatment' (Ciba Foundation 1959) and this definition was accepted by the Medical Research Council's Committee (1965). This is satisfactory for the ordinary, predominantly allergic, type of asthma with attacks of airways obstruction of fairly acute onset and short duration. We encounter difficulty in those cases in which the obstruction becomes persistent and severe with a response to bronchodilators or corticosteroids no greater than that encountered in chronic obstructive bronchitis. In such patients the original asthmatic history may be indefinite and they often develop a clinical picture indistinguishable from chronic obstructive bronchitis. The following case history illustrates the difficulty particularly well.

Man, aged 51

Having been perfectly fit, apart from a partial gastrectomy, this man suddenly started wheezing and coughing up scanty frothy mucoid sputum. He was persistently breathless but worse during regular winter exacerbations when he had increased volumes of yellow sputum. His ventilatory capacity was first measured at the age of 53 and his peak flow was 210 litres per minute. From then until his death from respiratory failure at the age of 62 he continued to have increasing shortness of breath, regular exacerba-

tions of bronchial infection for which he received frequent courses of antibiotics but in between which his sputum was mucoid and of small volume. His FEV varied from 0·6 to 1·3 l. His ECG showed some evidence of ischæmia. He also had systemic hypertension (blood pressure 200/100). In 1961 physiological studies showed FEV/VC 1·2/2·8 l.; total lung capacity 8·7 l.; residual volume 5·7 l.; $P\bar{v}CO_2$ 44 mmHg; DCO (single breath) 18·3 ml CO/min/mmHg. A few months before death his $P\bar{v}CO_2$ had risen to 57 mmHg. On the grounds of his large total lung capacity, reduction of diffusing capacity with small quantity of sputum between exacerbations and normal PCO_2 he resembled cases with severe emphysema (*see below*). At autopsy his lungs showed only moderate centrilobular emphysema but widespread blocking of bronchi with eosinophilia, mucus and marked muscular hypertrophy of the bronchial walls so that the appearances were characteristic of asthma.

It will be noted that I accept this case as chronic asthma on morbid anatomical grounds but there was certainly recurrent mucopurulent bronchitis as well. Our clinical definitions and diagnostic criteria are inadequate at present to distinguish correctly between such cases and cases of chronic obstructive bronchitis without an asthmatic basis. We may ultimately be able to base our definitions on morbid anatomy and devise diagnostic criteria that are applicable in life. Tests of bronchial reactivity to histamine or acetylcholine, as well as to bronchodilator agents such as the corticosteroid drugs and atropine, may help us (Altounyan 1964). This is a field of research that has been widely exploited on the Continent (De Vries *et al.* 1964) but which we have been slow to develop here.

The word emphysema used to be applied to any patient with airways obstruction resulting in an increase of residual volume as percentage of the total lung capacity and it was implicitly assumed that nearly all such cases, especially if resistant to bronchodilator drugs (Thomson & Hugh-Jones 1958) had widespread and severe damage to the pulmonary parenchyma. The incredulity with which obvious exceptions to this rule were regarded (Clinico-pathological Conference 1951, Baldwin *et al.* 1949) and lack of a clear definition of emphysema appears to have delayed recognition of severe chronic obstructive bronchitis without destructive emphysema which we now know to be quite common both in this country and in the USA (Burrows *et al.* 1964). The features of such cases which may enable many of them to be distinguished from some others with severe destructive emphysema have been fully described elsewhere (Fletcher *et al.* 1963, Burrows *et al.* 1964, Mitchell *et al.* 1964) (Table 5). Dornhorst's clinical description of patients with severe emphysema as 'pink and puffing' and

Table 5
Clinical characteristics of patients with severe emphysema or severe obstructive bronchitis

	Severe emphysema	*Obstructive bronchitis without severe emphysema*
Onset	Late adult	Childhood or early adult
Dyspnœa	+++	++ (may be slight)
Sputum	Scanty-mucoid	Profuse, often purulent
X-ray	Attenuated vessels	Full vessels
Cor pulmonale	Infrequent. Terminal	Frequent. Remittent
TLC	Increased	Normal or low
$PaCO_2$)	Normal or low	Raised
SaO_2)	Normal	Low
Gas transfer	Reduced	Normal
Polycythæmia	Rare	Occasional
Clinical picture	'Pink and puffing'	'Blue and bloated'

of those with chronic obstructive bronchitis as 'blue and bloated' remains a useful mnemonic. The distinction is neither so simple nor so complete as might be hoped. Cases presenting the 'blue and bloated' clinical picture may occasionally be found to have quite severe emphysema and, as in the patient described above, those who are 'pink and puffing' may occasionally have no emphysema. It is not to be expected that the anatomical state of the lung would be the sole determinant of the whole organism's response to airways obstruction. Jones (1965) has suggested that the response to exercise may be one factor. Patients with severe emphysema deprived of any pulmonary reserve tend to desaturate on exertion, thus receiving hypoxic stimulus to breathing: those without emphysema, by increasing ventilation to areas of structurally normal lung with impaired ventilation, may actually improve their oxygenation on exertion, thus lessening the hypoxic stimulus to the chemoreceptors. It is interesting that the patient I have described diagnosed as having emphysema but who had large areas of intact lung at autopsy increased his Pao_2 on exercise. The clinical picture in the patients without emphysema merges into that in patients who hypoventilate with only mild airways obstruction (McNicol & Pride 1965).

Ætiology of Chronic Obstructive Bronchitis

In epidemiological studies we assume that impairment of FEV normally indicates obstructive bronchitis. This may not be justified in individual cases in the clinic but in epidemiology, where we deal with groups, an occasional misdiagnosis is unimportant. A significant association between increase in sputum volume and impairment of ventilatory capacity has often been reported (Fletcher *et al.* 1959, Elmes *et al.* 1959, Fletcher & Tinker 1961, Mork 1962, Holland 1964) and since neither asthma nor emphysema is necessarily associated with increase in sputum volume the assumption that chronic bronchitis is the predominant cause of increased airways obstruction is justified.

Smoking and Chronic Obstructive Bronchitis

Many reports, which have been reviewed elsewhere (Royal College of Physicians 1962, Surgeon-General 1964), have shown that smokers of cigarettes have impaired ventilatory capacity compared with non-smokers and that ex-smokers and pipe smokers are relatively little affected. One curious feature of this impairment is that it has usually been found to be no greater in heavier than in lighter smokers (Higgins 1959, Fletcher *et al.* 1959, Fletcher & Tinker 1961, College of General Practitioners 1961, Huhti 1965) although there are some exceptions in which a small gradient with increasing cigarette consumption has been shown (Mork 1962, Holland *et al.* 1965). One explanation that has been advanced is that those smokers who find themselves adversely affected by the habit give up or cut down their consumption so that the heavier smokers are those more resistant to the effects of smoking while the lighter smokers are selectively the more susceptible. The difficulty that even gravely disabled subjects have in cutting down their smoking and the fact that we are mostly dealing in these surveys with the mild asymptomatic effects of smoking makes this hypothesis unlikely. The lack of difference between the ventilatory capacity of heavier and lighter smokers is all the more curious when we consider that those smokers who have simple bronchitis have on the average lower ventilatory capacities than those without such symptoms (Fletcher *et al.* 1959, Fletcher & Tinker 1961, Read & Selby 1961, Mork 1962) and the prevalence of simple bronchitis increases with increasing cigarette consumption. This apparent paradox implies that heavier smokers without simple bronchitis must have exceptionally high ventilatory capacities and needs further study. It would be hard to reconcile with the simple concept of inheritance of obstructive bronchitis and susceptibility to cigarette smoking proposed by Read & Selby (1961).

Whether or not susceptible smokers inherit their susceptibility to tobacco it is desirable from the point of view of prevention that we should detect them early and so concentrate our anti-smoking advice on those who most need it. It has been shown that in both smokers and non-smokers smoking one or two cigarettes tends to increase airways resistance (Nadel & Comroe 1961, Zamel *et al.* 1963), although Attinger *et al.* (1958) found a significant effect only in patients with airways obstruction. McDermott & Collins (1965) measured airways resistance by means of a body plethysmograph in some of the men in our survey before and after smoking a cigarette and found that subjects with mild symptoms of bronchitis had on the average a greater increase of resistance on smoking than those without such symptoms. My colleagues are now extending this work by carrying out such measurements on all the 900 men who are collaborating with us in the long-term prospective study to which I have referred. It will be of great interest not only to see whether McDermott & Collins' preliminary studies are confirmed on the larger group but also to watch the future progression of men who do and do not show increased sensitivity to tobacco smoke. A further possible extension of this study could be to attempt to identify in the laboratory the components of cigarette smoke that are responsible for the increase in airways resistance and perhaps even to design filters that might selectively remove them.

When smokers with simple bronchitis stop smoking their cough and sputum diminish but may not clear entirely, particularly if sputum is profuse, when it may continue in almost undiminished volume. The higher levels of ventilatory capacity found in ex-smokers compared with smokers suggest that giving up smoking should improve ventilatory capacity. Gregg (1964) reported that some but not all smokers who give up show an improvement in peak expiratory flow. In the past four years of my own prospective study 17 men who used to smoke 10 or more cigarettes daily have given up at such a time that we have at least two measurements of ventilatory capacity at six monthly intervals before and after they have given up smoking. None of these men has shown a significant change in ventilatory capacity. Two of the 11 men who were regularly producing sputum have shown a significant fall in sputum volume. In a collaborative study that has been carried out for the past five years by a group of chest physicians in a trial of chemotherapy in early chronic bronchitis (Medical Research Council 1965), it has been found that the rate of decline of ventilatory capacity is less steep in those who have stopped than in those who have continued to smoke. While giving up smoking may sometimes result in an improvement in ventilatory capacity in some cases the obstruction is irreversible.

Air Pollution and Chronic Obstructive Bronchitis

An urban factor, presumably air pollution, is assuredly incriminated in obstructive bronchitis. The symptom complex of productive cough, recurrent illnesses and dyspnœa, shows a steep rural/urban gradient (College of General Practitioners 1961) and mean ventilatory capacity was found by Holland *et al.* (1965) to be higher in rural than in London postmen both in smokers

and non-smokers and higher still in postmen in American cities. Although the cigarette appears to predispose powerfully to chronic obstructive bronchitis in this country there must be something else in our environment, most probably air pollution, perhaps aided by free admission of polluted air to unheated bedrooms, that hurries so many more smokers with simple bronchitis along the road to disability than in other countries with cleaner atmospheres.

The remarkably prompt effect of episodes of smog on both the clinical condition and mortality of patients with chronic bronchitis (Logan 1953, Bradley *et al.* 1958, Waller & Lawther 1957) shows that pollution must exert a direct effect and the exacerbations of infection that we witness after such episodes and which also increase mortality may be secondary effects. It is difficult to obtain direct evidence of any immediate effect of air pollution in normal subjects. Coulsen *et al.* (1965) found no significant relationship between variations in regular measurements of ventilatory function and variations of environmental pollutants, and only transient effects of exposure to high levels of pollution. In December 1962 we measured the FEV of 26 men on the last day of the severe cold smog of that month when there were high ambient levels of sulphur dioxide. None of these men showed any perceptible deviation from the FEV values recorded during the previous and subsequent weeks. These measurements were, however, taken in a warm office after the men had been at work for a few hours and it may be that any immediate effect had worn off. Dr J C Gilson (personal communication) once measured his own FEV during a severe smog episode in Lancashire and observed a significant fall; this was later followed by the development of bronchial infection. This seems to be the only recorded instance of the way in which smog may increase airways resistance before leading to infection.

The Relationship between
Bronchial Infection and Obstruction

There is a widespread belief that recurrent infection is the main cause of damage to the bronchial tree resulting in chronic increase in airways resistance or emphysema. This belief is based largely on retrospective studies by pathologists who find evidence of bronchiolar infection associated with emphysema (Reid 1954, Leopold & Gough 1957) and by clinicians whose patients often say that disabling dyspnœa followed an acute chest illness. Neither of these pieces of evidence is convincing. Pathologists cannot distinguish primary from secondary effects in their static view of events years before autopsy, nor can clinicians tell whether the patient who gives a history of acute deterioration really had a normal ventilatory capacity before the acute illness or was already seriously impaired but unaware of it. It is notable that ventilatory capacity has not been found to be lower in men with mucopurulent than in men with purulent sputum (Holland 1964). The only way in which this important relationship can be elucidated is by long-term follow-up studies. One such study is the co-operative trial of chemotherapy in early chronic bronchitis to which I have already referred (Medical Research Council 1965). Here no difference in the rate of decline of ventilatory capacity was found between those who had persistently mucoid sputum and those who occasionally or frequently had mucopurulent sputum. The average decline of ventilatory capacity with time was steeper in those men who had the more frequent or more protracted illnesses but this in fact tells us nothing about which caused which. There was no evidence that in these men ventilatory capacity tended to fall immediately after exacerbations of bronchitis. In my own prospective study of working men only transitory falls in ventilatory capacity following respiratory infections have been noted (Angel *et al.* 1965). If bronchial infection does encourage the development of chronic obstructive bronchitis it must usually do this gradually and by imperceptible stages rather than by sudden dramatic effect. Contrary to general belief there is at present no good evidence that bronchial infection leads to airways obstruction, but from the point of view of prevention it is clearly of great importance to establish the facts of this matter as we are trying to do in our prospective survey of working men.

The differences between patients with emphysema and obstructive bronchitis in the age of onset of disability and in the clinical characteristics suggest that separate ætiological factors must be concerned in the two diseases. They are significantly associated (Thurlbeck & Angus 1963) but the interpretation of this association is no easier than that of the association between bronchial infection and bronchial obstruction. The one may cause the other or both may have a common ætiological factor. One obvious factor here again is the ubiquitous cigarette, for destructive emphysema is rarely found in non-smokers. Auerbach *et al.* (1963) reported that 'rupture of alveolar septums', an abnormality presumably closely related to emphysema, was almost exclusively found in cigarette smokers and with increasing frequency with increasing cigarette consumption. It may be that smoking only affects the prevalence of emphysema through the

mediation of bronchitis with its coughing and recurrent infection, but the possibility of direct action has been suggested by Miller & Bondurant (1962) who found that cigarette smoke affected the alveolar lining complex in such a way as to encourage the emptying of smaller lung spaces into larger spaces, a change which might encourage the formation of emphysema. Our lack of methods for early diagnosis in life renders systematic epidemiological study extremely difficult and this is one reason why we know so little about the ætiology of the various types of emphysema. The mechanism by which these different types, such as panlobular, centrilobular, focal and peri-cicatricial, are produced must be different in many respects but at present we can only construct unconvincing retrospective hypotheses about them.

Pathogenetic Conclusions

I have adduced evidence that air pollution and smoking may play a part, probably independently, in causing all three components of the bronchitis syndrome: hypersecretion, infection and obstruction. Infection by bacteria or viruses can apparently initiate prolonged hypersecretion and this may also increase susceptibility to infection so that a vicious circle may be started. Structural damage to the bronchi may eventually lead to persistent infection but this by itself carries no threat to survival. It is increase in airways resistance which eventually kills our patients. This I believe is neither a consequence of hypersecretion nor of bronchial infection but rather a primary reaction to environmental irritants in subjects whose bronchial reactivity is analogous to that of the asthmatic but different in that it is less obviously mediated through allergy and is much more persistent. In patients without airways obstruction recurrent exacerbations of infection have only a nuisance value, but in those with obstruction the increase of secretion and perhaps associated mucosal swelling may raise the resistance to air flow to dangerous levels and although it appears to be the infection that menaces life it is really the pre-existing obstruction from bronchitis or emphysema that is so dangerous.

Prevention and Treatment of Chronic Bronchitis

I now turn to consider the relevance of what I have been saying to the preventive and curative treatment of chronic bronchitis and emphysema.

The individual physician can do little about generalized air pollution. Those who live in polluted cities may protect their patients by advising them to keep their bedroom windows shut, at least in winter, and by staying at home in foggy weather. No clear evidence has yet been provided that the neutralization of the acid content of smog by the ammonia liberated from an Airwick bottle is beneficial though the result may be pleasant, nor has it been possible to demonstrate any objective benefit from the use of any form of smog mask. In advanced disease a change of residence from urban to rural environment has not had any notable effect on my patients' disability but it spares them the hazards of smogs. Evidence from the smog of December 1962 that the reduction of the smokiness of London air may already be rendering its smogs less dangerous is uncertain but is encouraging (Lawther 1963). Further encouragement in the operation of the Clean Air Act is what the authorities need from our profession.

Even if we could lower urban air pollution to levels found in rural areas the cigarette would still, as it does there, induce disabling bronchitis in large numbers of men and women and we have to address ourselves to the task of overcoming this major agent of disease. There are three lines of attack:

(1) General reduction or, ideally, abandonment of cigarette smoking. That the addiction to the cigarette can be overcome by an important proportion of smokers is shown by the example of doctors in this and other countries (Royal College of Physicians 1962, Gardiner & Taylor 1964). Evidence of the similar reduction of smoking in non-medical graduates in Edinburgh (Lynch 1963) suggests that this is due to intelligence rather than proximity to the dire consequences of cigarette smoking and that the example of the doctors may be relevant only to a small proportion of the general public with above average intelligence. In fact, since the Royal College of Physicians report was published and the Ministry of Health has embarked on a slowly growing campaign of health education about cigarette smoking, the previous rate of increase in cigarette consumption has tended to decline by about 10% in men although it has continued to rise with little check among women (Fig 1). Two brief attempts at intensive local public education in Edinburgh and Dunfermline (Cartwright *et al.* 1960, Scottish Department of Health 1964, unpublished report) were entirely ineffective. It is conceivable that with better understanding of the motivation of smoking, an understanding which is now being sought through detailed population surveys by the Central Office of Information, we might achieve methods of persuasion that would be more effective than any we have at present. It is

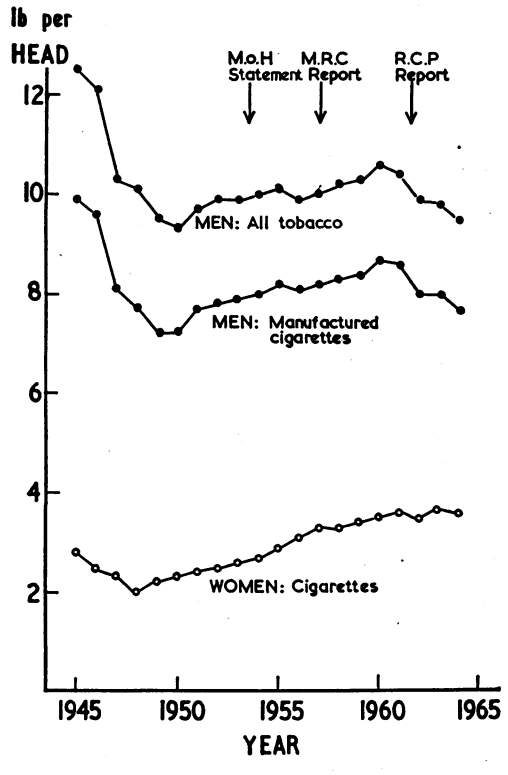

Fig 1 *Tobacco consumption by adults in the UK 1945–64*

also possible that the recent overt Government action against advertising of cigarettes on independent television, if followed up by still further legislative prohibition of advertising, might begin to have an effect, but it is unlikely to be large. I believe that only a tax increase sufficient to make a single cigarette an expensive luxury, especially if coupled with a reduction in the cost of pipe and cigar tobacco, would have any significant effect upon the smoking habits of the general public.

(2) We may learn how to identify future cases of obstructive bronchitis at a stage before irreversible damage has been done to the lungs. Gregg (1964) has shown how the Wright peak flow meter can be used to detect minor degrees of ventilatory impairment in smokers without symptoms. We hope to discover from our own survey how far increased sensitivity to cigarette smoke is associated with such mild impairment. Long follow up will be needed to determine whether subjects detected in this way develop obstructive bronchitis. Here is a great opening for research in general practice. Even if we could detect early cases in this way we would still be left with no sure means of persuading these still healthy but susceptible smokers to stop their dangerous habit.

(3) More hopefully, if we could identify the components of cigarette smoke responsible for the irritation of the bronchi which leads to chronic bronchitis, it might be possible either to modify cigarette tobacco in some way that would reduce the irritant component of the smoke without removing its pleasurable effects or to devise filters that would do the same.

The obstinacy of our present problem is shown by the difficulty we have in persuading our patients with chronic bronchitis and emphysema to stop smoking. Among patients attending a bronchitis clinic in London and an emphysema clinic in Chicago with severe obstructive bronchitis or emphysema, 53% were still smoking cigarettes (Fletcher *et al.* 1964). A recent survey of the results of anti-smoking clinics which have been set up all over the country in the past three years showed an average success rate (the proportion who were no longer smoking three months after attending the clinic) of 29%, ranging from 83% at a church clinic in Glasgow to 7% at one local authority clinic in London (Cruickshank 1964). No greater success was achieved among the 400 patients attending clinics in the Medical Research Council's trial of chemotherapy in early chronic bronchitis. Those who attend such clinics or anti-smoking clinics are a sample selected from the general population as being those with a particularly keen desire to stop. No special technique has yet been discovered that appears to increase the success rate. The earlier hope of the lobeline compounds has been disappointing (British Tuberculosis Association 1963). In one clinic hypnotherapy was found to be no more successful than placebo tablets. All the doctors who had worked in anti-smoking clinics felt that their main difficulty stemmed from the forces of social custom and advertisement which pressed upon their patients when outside the clinic. While freedom of advertisement continues to indicate that the Government is not deeply concerned in this problem it will remain impossible to mount an effective campaign against the cigarette and to change the image of the smoker from that of the carefree social success to that of the unfortunate addict.

There is no doubt that prophylactic chemotherapy can reduce the number and duration of exacerbations of infection in established cases of chronic bronchitis (*Brit. med. J.* 1964) but the MRC trial of prophylactic chemotherapy showed only a small effect on duration of illness in early cases of chronic bronchitis and no effect on

the rate of decline of FEV (Fletcher 1964*b*). It seems unlikely that control of bacterial infection can play an important role in the prevention of disabling bronchitis.

This brings me to the question of treatment. First, by the time we are consulted by patients with chronic bronchitis irreparable damage has usually been done. We can provide some symptomatic relief and often postpone death but we cannot reverse the course of the disease. This is why we must concentrate our efforts on prevention. The social class gradient demonstrates that three-quarters of the cases of bronchitis that occur in Britain today are probably preventable if only we can unravel the ætiological problems that I have been discussing.

Secondly, I wish to emphasize the importance of measuring the effects of our therapeutic measures. In respect of respiratory symptoms there is a wide divorce between the subjective statements of our patients and objective tests of the disorders of which they complain (Fletcher 1963). Simple methods for measuring sputum, for assessing its purulence and for measuring airways obstruction have been standardized for epidemiological studies (Medical Research Council 1965) and are readily available for the clinician. The physician who today treats patients with bronchitis and emphysema without measuring their responses is like a physician who treats hypertension without using a sphygmomanometer.

My third point is humanitarian rather than scientific. Most patients with severe bronchitis are distressed and anxious. Even if we can give them no measurable objective help we can sustain their morale by kindness and encouragement and this they may need more than any small objective aid that we can give them. Dr Elmes and I once found (Elmes *et al.* 1957) that lactose tablets were better than no tablets in helping bronchitics to keep at work during their exacerbations and that oxytetracycline tablets were not significantly better.

Because of our failure to offer a cure to our patients a bronchitis clinic may be depressing, especially with the approach of autumnal fogs, but our patients are grateful for the crumbs of benefit that we can offer and the reassurance, even if unjustified, that we give them. In this task general practitioners and physicians must collaborate to help the vast armies of bronchitics in England today. Since cure is unattainable prevention must be our major concern and here the main enemy we have identified is the cigarette.

Just over three hundred years ago Dr Tobias Venner of Bath, a physician whose vigorous pen is reminiscent of that of Philip Ellman, published his 'Via Recta Ad Vitam Longam' to which he annexed 'An Accurate Treatise Concerning Tobacco'. His reasoning was not scientific and he had no statistics to support his conclusions but his vision was clear and his treatise ends thus:

'I wish them that desire to have *mentem sanam in corpore sano*, altogether to abandon *insanum præposterumque Tobacci usum*. This is all which seemed good unto me to be written of Tobacco's fume, partly for shewing the right manner of using it, but especially for reproving the too too licentious, liberall, and intempestive taking of it, which very many in these dayes, do to their own ruine lewdly, and for want of better employment, foolishly affect.'

We now have incontrovertible evidence of the ruin wrought by the cigarette. It is up to us to fulfil Dr Venner's wish by effective action.

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