JOINT MEETING No. 5

Section of Pathology with Section of Epidemiology and Preventive Medicine

Chairman—MAURICE MITMAN, M.D., F.R.C.P., D.P.H.
(President of the Section of Epidemiology)

[*February* 21, 1956]

SYMPOSIUM: CHRONIC BRONCHITIS

Dr. D. D. Reid (Reader in Epidemiology and Vital Statistics, Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine):

General Epidemiology of Chronic Bronchitis

In these introductory remarks, I take as a working definition of the disease—"that condition which is described as 'chronic bronchitis' by general practitioners when they complete certificates of cause of incapacity or death"—for, in the initial stages of an epidemiological study, we are entirely dependent on the broad pictures which such data provide.

Fig. 1 shows that chronic bronchitis, as thus defined, ranks in importance as a cause of death in this country with arteriosclerotic heart disease: among the General Post Office staff, for example, it is the recorded cause of 15% of premature retirements from work on grounds of ill-health (Roberts and Reid, 1954). Like coronary heart disease and cancer of the lung, it is largely a disease of males and accounts, with the other two, for most of the ominous middle-age excess in contemporary male mortality.

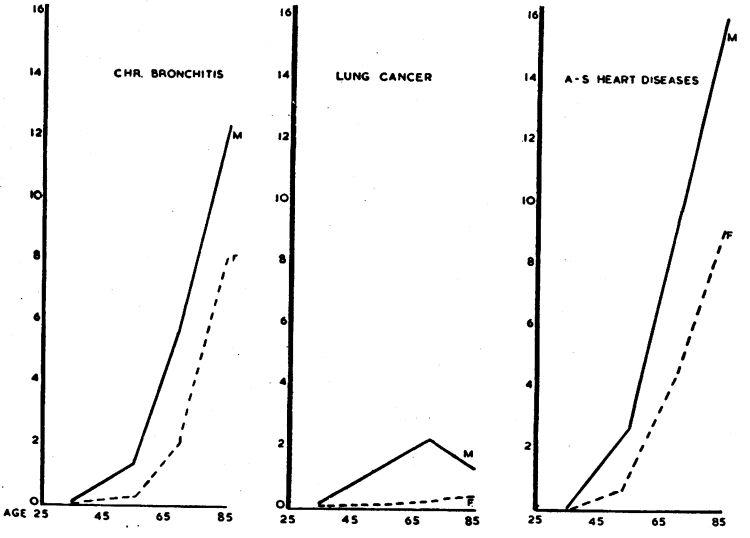

FIG. 1.—England and Wales 1951 death rates/1,000 p.a.

Since it is so markedly a disease of males, and since this symposium has an international flavour, we can start our search for clues about causation by comparing, as in Fig. 2, the crude male death rates ascribed to bronchitis in the countries of North-West Europe. There is a remarkable gradient from the very low rates of Norway and Denmark, the slightly higher rates of Sweden, France and Switzerland, and the greater mortality in Western Germany, the Netherlands and Belgium, to the peak rates of the British Isles in general and of England and Wales in particular. In terms of relative frequency at least, chronic bronchitis is a modern analogue of the "English sweats" of the sixteenth century, and it is a happy coincidence that one of the best descriptions of that other epidemic respiratory

catarrh came in 1580 from Professor Mulder's predecessor in the faculty of medicine at Leiden, Peter Foreest (Withington, 1894).

Concentrating on England and Wales, we see in Fig. 3 that, although there is a general increase in the death rates as we pass from South-East to North-West, the main concentrations

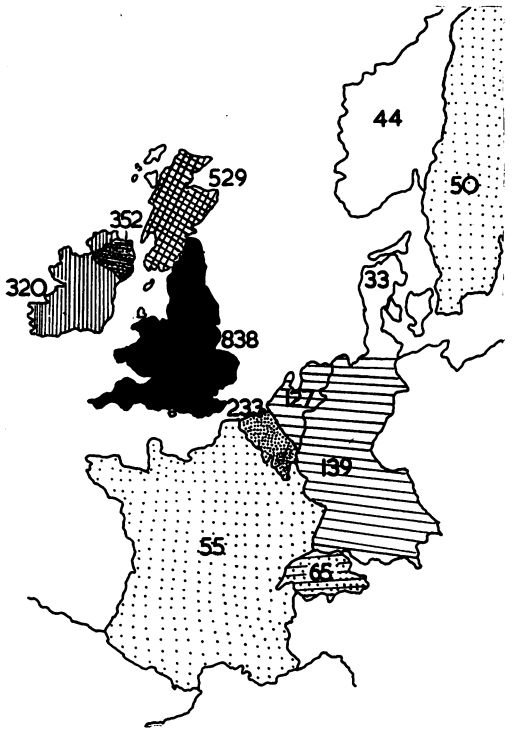

FIG. 2.—Bronchitis mortality in N.W. Europe. Crude male death rates/million p.a., 1952.

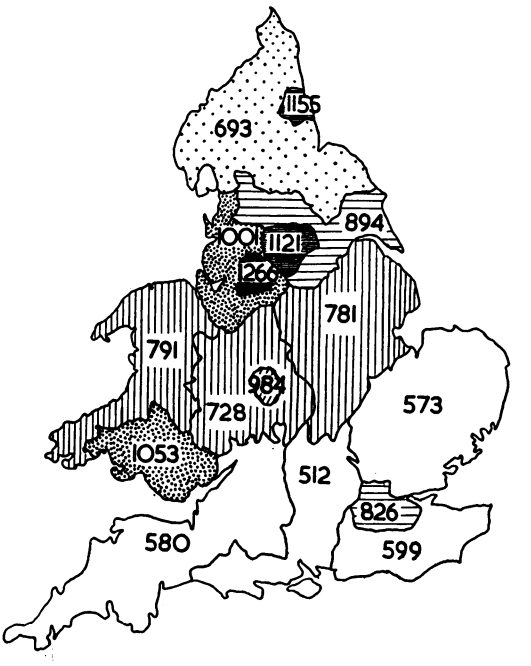

FIG. 3.—Bronchitis mortality in England and Wales. Rates per million, 1950.

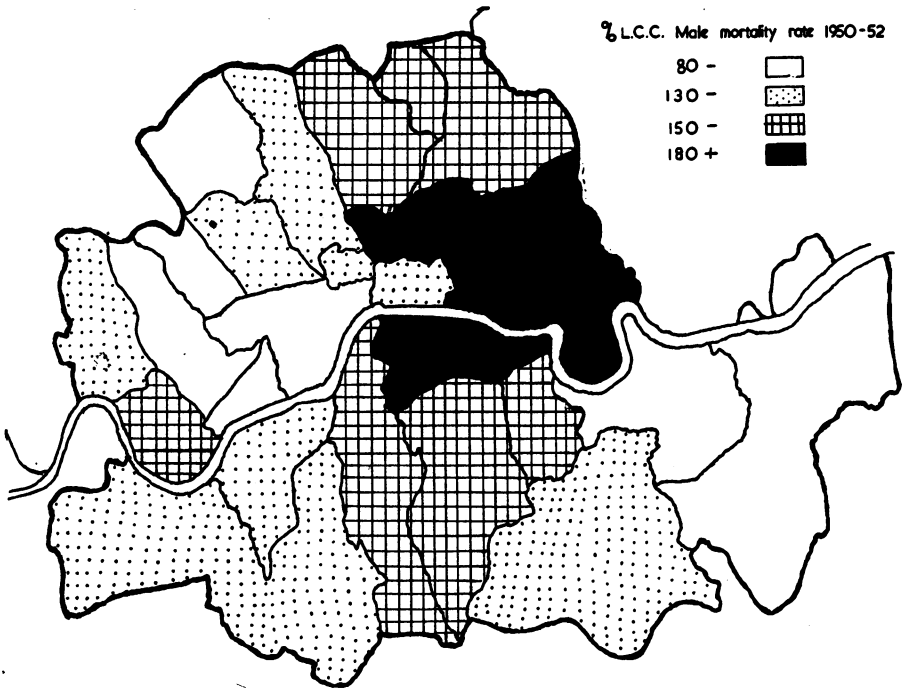

FIG. 4.—Bronchitis mortality in London. Male mortality ratio 1950–52.

of high bronchitis mortality are in the great industrial conurbations which stand out, even in the North-West, from the surrounding districts.

Even within an urban area like the County of London, where climatic conditions of temperature and humidity are reasonably uniform, there is an area of excessive bronchitic mortality in the central and north-eastern parts of the county (Fig. 4).

Interpretation of these spatial contrasts is extremely difficult. The black areas certainly are the districts most affected by industrial and domestic smoke pollution. The smog of 1952, for example, was most intense there. But equally, they house the semi-skilled artisans and labourers who are exposed by their jobs to physical exhaustion, to the weather and to industrial dust and fumes. With their wives, these men share the risks of multiple infections in congested areas and overcrowded homes. These social and environmental factors, together with inadequate diet and medical care, have all been indicted as causes of the steep social-class gradient in both male and female mortality rates which is so striking a feature of chronic bronchitis.

In a disease where many causative factors are implicated, the problem is to try to isolate and measure the effects of even a few of them. Some of the inherent difficulties can be resolved, however, by what has been termed the "artichoke" principle in scientific investigation. The general idea of this approach in epidemiological enquiry is to measure the isolated effect of one factor at a time, by comparing the incidence of disease in two population groups where all relevant factors except that one have been kept constant. The same process is continued by dividing and comparing the population in different ways until, factor by factor, the problem has been dissected.

The staff of the General Post Office forms a particularly suitable population for such a method. It includes men and women doing standardized jobs at similar rates of pay spread fairly evenly over the country, uniformly selected and under the overall medical supervision of the Treasury Medical Service.

Thus we can isolate the effect of sex differences by comparing the incidence of bronchitis in men and women of the same age, doing similar indoor office jobs, in the same district at the same time. The experience of male and female London office workers set out in Fig. 5 shows that the male excess in later life, seen in sickness as in death, cannot be entirely explained by differences in climatic exposure, range of infective contacts or the physical demands of men's and women's work. Whether it is simply another aspect of male biological inferiority or, as Oswald and Medvei (1955) have recently suggested, the result of habits like heavy smoking, remains to be seen.

Similarly, we can concentrate on the effect of job differences on bronchitis morbidity by comparing, as in Fig. 6, attack rates in men doing physically more arduous outdoor work as

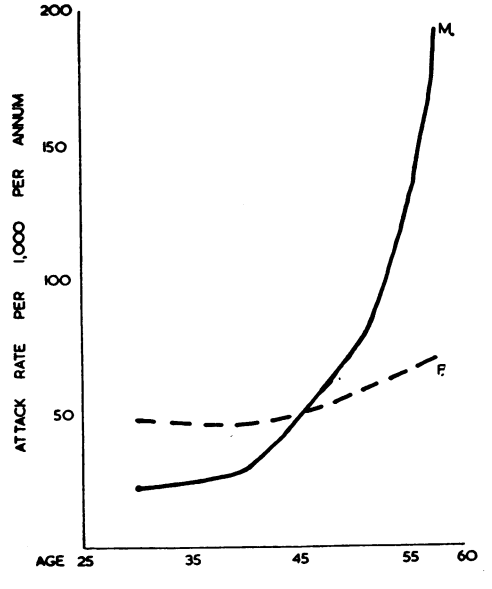

FIG. 5.—Bronchitis in London clerical workers.

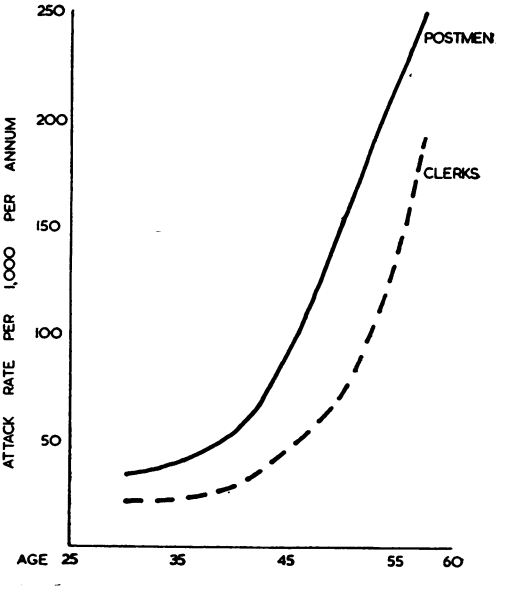

FIG. 6.—Bronchitis in male London postal workers.

postmen with those in men of the same age in the same district at the same time but working as clerks. In so far as absence from work is a reasonable measure of incidence, bronchitis is much more frequent in the postmen who spend much of their lives outdoors in London. Postmen in Greater London share the same climate, the same job and the similar social circumstances which go with standard rates of pay. Since the doctors of the Treasury Medical Service try to ensure reasonably consistent clinical standards of invaliding from the postal service, we can use the bronchitis invaliding rate as an index of clinical response to the street environment in different parts of London. Thus in Fig. 7 we divide the whole area, through the City centre, into four quadrants and compare the annual bronchitis invaliding rates for the central area and each of these quadrants. If we then assume, as Stocks did in his study of cancer of the lung (Stocks, 1952), that the prevailing west-south-west wind will cause a build-up in smoke pollution over the centre and north-east of the area, the gradient in rates from South-West (2·6) to North-East (4·5), is, to say the least, suggestive.

Finally, lest we become hypnotized by the idea that smoke pollution is the all-important factor, we can compare in Fig. 8 the trends in national male mortality rates from chronic bronchitis with contemporary trends in sickness-absence rates in Post Office workers spread over the whole country. These absences are largely due to virus infections of the respiratory tract and the close time-correlation seen here re-emphasises the role of epidemic infections, such as the influenza outbreak of 1951, in causing death in the chronic bronchitic. One might also note the apparent failure of antibiotic therapy to achieve any major consistent drop in bronchitis death rates in recent years.

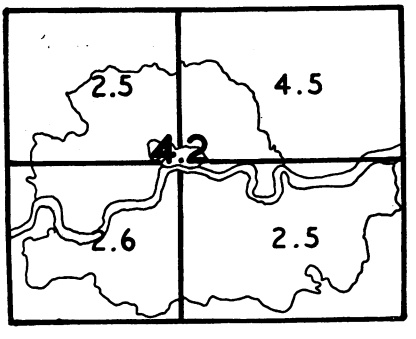

FIG. 7.—Bronchitis invaliding rates in London postmen (per 1,000 p.a.).

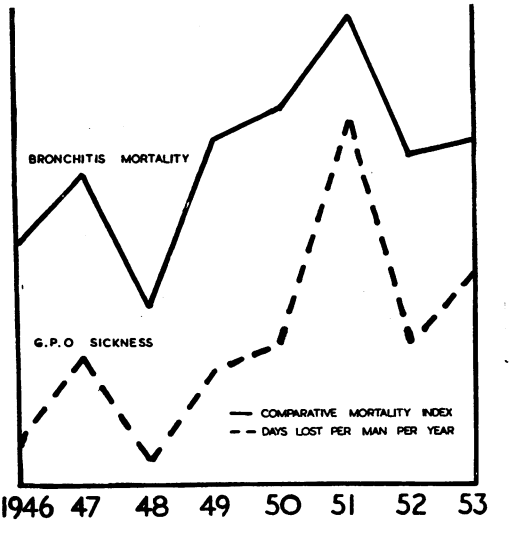

FIG. 8.—Trends in bronchitis mortality and total sickness absence rates.

What are these scraps of epidemiological evidence worth? One might suggest that chronic bronchitis is a disease of the industrial countries of North-West Europe in general and of England in particular. Although death from chronic bronchitis is most frequent in the poorer working-class districts of the industrial cities, smoke pollution seems to have an effect on sickness which is independent of differences in nature of work and standard of living. Again, the undue susceptibility of the middle-aged male cannot be entirely explained by differences between the contacts, physical demands or climatic exposures of men's and women's work. Finally, whatever the predisposing causes, whether of environment, physique or personal habit, the common respiratory infections appear to be major precipitants of serious disability and death in a disease whose importance is matched only by our ignorance of it.

I am indebted to Dr. W. Chiesman of the Treasury Medical Service for his help and for permission to publish some of these data.

SUMMARY

A survey is made of epidemiological evidence on the numerical importance of chronic bronchitis as a cause of death in various parts of North-West Europe and as a cause of sickness in the staff of the General Post Office in London. The unusually high frequency of death from chronic bronchitis among the males of the industrial areas of England is remarked upon, and some evidence for the ætiological importance of smoke pollution and of infection is reviewed.

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Dr. Lynne Reid (Institute of Diseases of the Chest, London):

Pathology of Chronic Bronchitis

The morbid anatomy of chronic bronchitis cannot yet be presented as a complete picture, which relates its beginnings and progression to the causes which may operate, for these causal factors are still largely unknown. Further, the disease has no specific or diagnostic lesion: its most characteristic feature seems rather to be the pattern of involvement of the lung. Even if in the early stages of chronic bronchitis the changes are confined to the bronchi, in the later stages pathological changes are also present in the bronchioles and respiratory part of the lung.

The earliest and most constant clinical feature in chronic bronchitis is the production of sputum, which reflects hypersecretion of bronchial mucus. Mucus is normally secreted from goblet cells in the bronchial epithelium and from mucous glands in the walls of the bronchi. The glands have the same distribution as the cartilage, and, like the plates of cartilage, are fewer in number in the more peripheral bronchi. The number of goblet cells in the epithelium also decreases progressively towards the periphery, so that there is only an occasional one in the wall of a bronchiole. Except in the bronchi, therefore, there are relatively few mucus-producing cells in the normal lung.

In chronic bronchitis the increased production of mucus is reflected by an increase in the number of cells which contain mucus. The mucus may be present only in the form of mucinogen granules at the base of the cell, or the cells may be distended with mucus or in process of discharging it. There is also an increase in the number of goblet cells in the ducts of the mucous glands and the amount of mucinous material in the cells of the acini is greater. The number of goblet cells in the bronchioles is also increased, although the changes here may vary in different parts of the lung. Usually, however, in operation or autopsy specimens from patients in whom chronic bronchitis has been present for some years, changes are also present in the peripheral part of the lung, within the secondary lobules. The changes here are varied. There may be acute purulent bronchiolitis, or there may be scarring which suggests previous damage to bronchioles. The bronchioles may be dilated or obliterated, or the combination of dilatation and obliteration may convert them into cysts. The alveoli also show a variety of changes: pneumonic consolidation, collapse, abscess formation, emphysema, œdema, fibrosis. These changes in the bronchioles and alveoli, although listed separately, are related. The changes include some which are acute and others which are chronic, and some which could resolve and others which have already produced irreversible damage.

These changes may be illustrated by the findings in serial histological sections cut through a block of tissue which was taken at autopsy from a part of a lung which macroscopically appeared to be relatively normal. The patient was a man of 64 who had a history of chronic bronchitis over many years. He had noticed shortness of breath for six years before his death, and he had been in hospital several times because of exacerbation of his symptoms. Three secondary lobules were traced through the serial sections. The first lobule showed bronchiolectasis—the bronchiole expanded into a cystic area which was surrounded by scarred, collapsed lung, in which one of the side bronchioles ended blindly. In the second lobule there was a small focus of pneumonia around one of the bronchioles, and adjacent to another bronchiole there was a microscopic abscess cavity which had ulcerated the bronchiolar wall at one point. The third lobule, although of approximately the same diameter as the other two, was in fact the scarred remnant of a considerably larger volume of lung. An elastic-tissue and van Gieson stain showed the remains of collapsed lung with the dilated branches of the bronchial tree in the centre. The regular arrangement of the muscle fibres showed that ulceration had played little part and that dilatation was the main reason for the increase in diameter.

The third of these lobules had been palpable in the lung as a firm nodule about the size of a cherry stone. In some patients with chronic bronchitis many such nodules are palpable: to gain some idea of their frequency, and of the pathological changes which they represent,

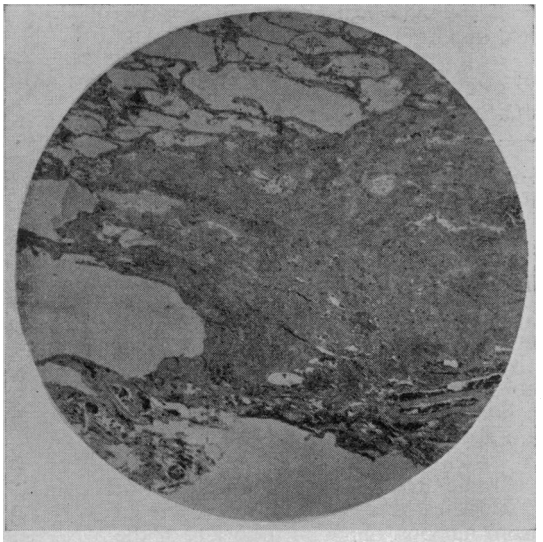

FIG. 1.

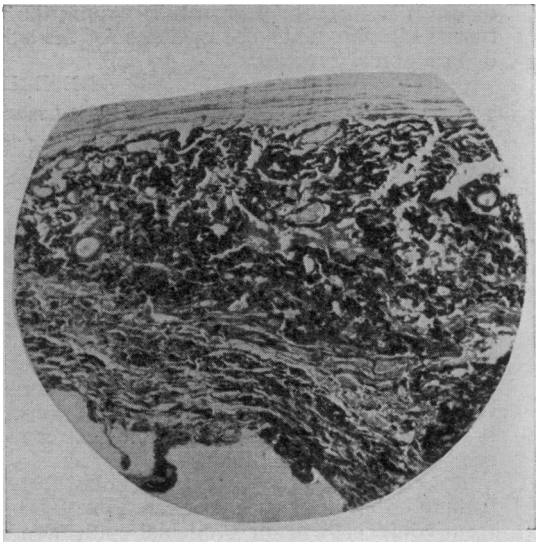

FIG. 2.

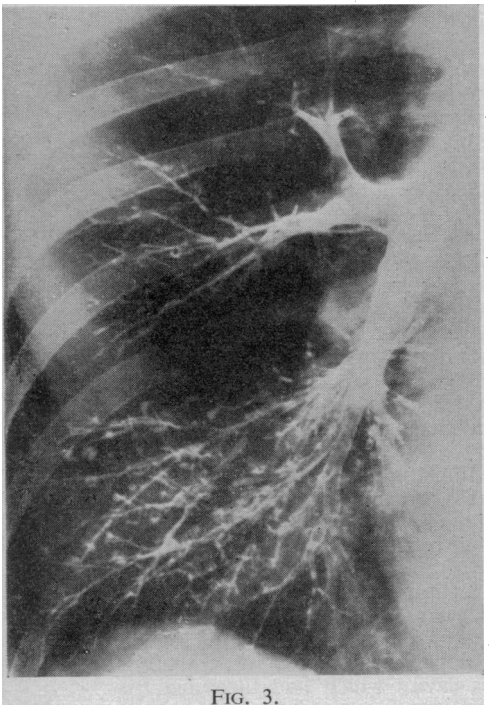

FIG. 3.

FIG. 1.—Nodule of condensed lung showing homogeneous appearance when stained with hæmatoxylin and eosin. It lies deep in the lung. × 12·5.

FIG. 2.—Subpleural nodule stained to show elastic fibres (black), and illustrating the condensed pattern of the lung. (Verhoeff and van Gieson stain.) × 20.

FIG. 3.—Right bronchogram showing pools of radio-opaque material, several millimetres in diameter, in the peripheral part of the lung of a patient with chronic bronchitis.

thirty-two lobes from twelve patients with chronic bronchitis were studied. It was found that the diameter of the nodules ranges from several millimetres to one and a half centimetres. Deep in the lung they usually feel spherical; but in the subpleural region they are often flatter, and may be so shallow that they are dismissed as pleural thickening. These lesions look

more impressive in thin stained sections than they do in the gross specimen: in the latter, if they are surrounded by normal-looking lung they are not obvious, while if there is emphysema around them they are usually overlooked because the emphysema is more impressive. The nodules are not rare, but they are irregularly distributed: for example, in one patient eighteen nodules were counted in one lobe and five in another, while in three lobes there were none at all. Histologically these nodules appear homogeneous when stained with hæmatoxylin and eosin (Fig. 1). An elastic tissue and van Gieson stain is necessary to distinguish pneumonia from collapse (Fig. 2). Of the nodules studied histologically about one-half showed predominantly pneumonia, rather more than one-quarter showed predominantly collapse, and in the remainder fibrosis was so dense that the nature of the change could only be recognized with difficulty. In two-thirds of the total fibrosis was considerable.

These nodules, then, represent localized changes of different ages in the peripheral part of the lung. Although much of the acute change doubtless resolves, the dense fibrosis in some nodules suggests that scarring is not an infrequent result. The volume of normal lung which these nodules represent is considerably greater than their own final volume.

Bronchography in patients with chronic bronchitis readily shows the results of these pathological changes. There are two main bronchographic changes in the peripheral parts of their lungs. The first is the absence of peripheral filling. Deficient peripheral filling may result from technical inadequacy, or from sputum in the lumen of the bronchial tree, in which case the ending is usually squared. Often, however, and particularly when the end of a bronchiole is rounded, the failure to fill results from the obliteration of the bronchiole in a scar. The second feature is the presence of peripheral pools of contrast medium several millimetres in diameter (Fig. 3). From examination of the lung these pools can be shown to represent bronchiolectasis.

I have presented the pathological changes in chronic bronchitis in two parts; this has the convenience of corresponding approximately to an anatomical division. The first part illustrates the disturbance of mucus secretion and is concerned mainly with the bronchi, while the second represents the changes in the respiratory part of the lung, that is, in the bronchioles and alveoli. This division has a further use; in the present state of our knowledge of chronic bronchitis, it is useful, although doubtless an oversimplification, to think of these two aspects as posing separate questions. The disturbance of mucus secretion presents the problem of the fundamental cause or causes of chronic bronchitis; on the other hand, the increasing involvement of the peripheral part of the lung presents us with the problem of the clinical progression of the condition. The various lesions that have been demonstrated and the different factors that influence them, such as infection, climatic conditions and occupational environment, should therefore be assessed separately in relation to the part which they play in these different phases of the disease.

Professor Dr. J. Mulder (Clinic for Internal Medicine, University Hospital, Leiden, Holland):

Bacteriology of Bronchitis

I. Chronic Bronchitis

Chronic bronchitis is a clinical diagnosis which relates to a number of different inflammatory conditions of the bronchi. Excluding tuberculous bronchitis and other rare forms of bronchitis, e.g. bronchomycosis, one can distinguish four groups of chronic bronchitis.

(A) "Allergic" bronchitis (eosinophilic, asthmatic, or bronchospastic bronchitis; Laennec's *catarrhe sec*). Patients with "allergic" bronchitis present the following manifestations: (1) Chronic cough. (2) Expectoration of viscid, "mucoid" sputum, which is usually scanty and which microscopically shows predominance of eosinophil leucocytes and macrophages; these sputa do not show a pathogenic bacterial flora. (3) Sometimes, on bronchographic examination, a spastic bronchial tree can be shown to exist, without bronchiectasis or bronchial deformation. (4) Some of the patients never suffer from attacks of bronchospasm (asthma); others have a number of these attacks, and some develop chronic bronchospasm which often leads to severe emphysema and gives rise, after a varying number of years, to manifestations of cor pulmonale.

(B) The second group, which is not common, comprises patients suffering from chronic mucopurulent bronchitis, without evidence of allergic bronchitis. The manifestations are the following: (1) Chronic productive cough. (2) The production of mucopurulent sputum which always contains a pathogenic aerobic flora. (3) Absence of eosinophils in the sputum and of bronchospasm. (4) Absence of general emphysema. (5) Rapid development of bronchiectasis and bronchial deformation. (6) Clubbing of the fingers. (7) Development of amyloidosis in long-standing cases.

(C) The third group, which includes the greatest number of patients suffering from chronic bronchitis, is a combination of groups A and B. In our material about 80% of patients suffering from bronchiectasis belong to this group. In many cases the symptoms of asthmatic bronchitis prevail, in other cases those of mucopurulent bronchitis. Sometimes the underlying asthmatic condition becomes manifest only after a period of treatment with antibiotics: in these cases the patients continue to expectorate mucoid sputum containing eosinophil leucocytes. During and after antibacterial treatment some patients develop a very severe bronchospasm, which may be fatal.

(D) The fourth group is made up of cases of chronic fetid mucopurulent bronchitis and is not strictly a separate one. The sputum is foul and bacteriologically shows a multiple, partly anaerobic flora. Some cases are associated with ozæna (tracheal and bronchial ozæna) and do not develop bronchiectasis. Most cases belong to the group of mucopurulent bronchitis and are nearly always associated with bronchiectasis. There is no correlation between the appearance of fetid sputum and the diameter of the diseased bronchi. Fetid sputum most probably only appears in cases in which the ciliated bronchial epithelium undergoes metaplasia, with the development of squamous epithelium (Mulder and Hers, 1955).

A screening method for the investigation of eosinophilia in the sputum.—For many years we have used the following technique for demonstrating eosinophil leucocytes: fragments of sputum are washed in buffered saline and stained in a solution of 0·05 gram of eosin and 1·0 ml. of 40% formalin in 100 ml. of distilled water (Zollikofer's solution). The sputum is gently compressed under a cover glass and studied at low magnification. The eosinophilic granules are stained dark red. The neutrophil cells are uncoloured but clearly visible.

The bacteriological flora in mucopurulent bronchitis. Technique of the bacteriological examination of the sputum.—We believe that a preliminary Gram stain of the sputum is necessary in order to obtain correct results. In the first place the Gram stain serves as a control to ensure that the sputum has been properly washed, for pharyngeal or oral mucus can be identified by the presence of squamous epithelial cells, which usually contain micro-organisms. The presence of oral and pharyngeal flora is a further indication of inadequate washing of the sputum. The second reason for the preparation of a Gram stain is the fact that the stained preparation may reveal bacteria which may not grow well on artificial media, e.g. *Hæmophilus influenzæ*, Klebsiella, and anaerobic organisms. The investigation is carried out on sputum which has been expectorated into a Petri dish. The specimen is examined against a black background. A very small piece is isolated with a loop and washed successively in three Petri dishes containing buffered saline. The piece is then dried as much as possible by pressing out the saline, as smears of wet sputum do not give reliable microscopic pictures. Smears are made on glass slides: duplicate preparations are stained by Gram's method and with methylene blue. Sometimes, especially in chronic infections with *H. influenzæ*, micro-organisms can be seen only within the leucocytes. In general, a tentative identification of the pathogenic genera present in the sputum can be made with reasonable certainty from the Gram preparation.

Culture media.—We use for each culture blood-agar and Levinthal-agar (plates and tubes) and also a tube containing blood-serum broth for the selective growth of pneumococci (this medium is as reliable as mouse inoculation).

Fetid sputum should be cultivated anaerobically since *H. influenzæ* which may be present in these sputa grows only anaerobically in the primary culture.

The importance of bacteriological examination of sputum from cases of bacterial bronchitis is that an adequate antibiotic can be chosen for treatment. Antibiotic treatment should be given (1) before bronchographic examination is done, in order to rid the bronchial tree of as much mucopurulent exudate as possible, so that the exudate will not prevent proper filling of the bronchi by the contrast medium; (2) before and after surgical treatment of bronchiectatic lobes or segments, and (3) when the condition is too extensive for surgical treatment.

Incidence of pathogenic genera in cases of mucopurulent bronchitis (Tables I and II). H. influenzæ *group.*—From Tables I and II it can be seen that the *H. influenzæ* group is the most important group of organisms pathogenic to the mucosa of the respiratory tract (Mulder *et al.*, 1952; May, 1954). 95% of all strains isolated from adults are unencapsulated and the remaining 5% are encapsulated. Most encapsulated strains belong to the Pittman subgroups B and F; other subgroups are occasionally present. The underlying mechanism of this distribution is unknown but merits further research. The finding of a subgroup B infection in the bronchi is also important from an epidemiological point of view because it shows that adults may carry these strains and may in this way form a source for cases of septicæmia, meningitis and phlegmonous laryngitis in children below the age of 10. Unencapsulated *H. influenzæ* is definitely pathogenic in the airways: its elimination by antibiotics causes the disappearance of the toxic symptoms of inflammation and halts the production of mucopurulent sputum (Mulder *et al.*, 1952). In chronic cases, recurrences or relapses of inflammation are very common.

TABLE I*.—BACTERIAL FINDINGS IN ACUTE AND CHRONIC MUCOPURULENT BRONCHITIS (1946–1950)

Clinical diagnosis	Genus															
	H. influenzæ	Pneumococci**	Neisseria	Klebsiella	*E. coli*	*Staph. aureus*	*Strept. hæmolyticus*	Proteus	*Ps. pyocyanea*	Anaerobic	*H. influenzæ* + Pneum.**	*H. influenzæ* + Neiss.	*H. influenzæ* + Klebs.	*H. influenzæ* + alpha hæmol. strept.	*H. influenzæ* + *Staph. aureus*	*H. influenzæ* + *E. coli*
Acute mucopurulent bronchitis	19	1	3								3				1	
Acute mucopurulent bronchiolitis	2															
Asthmatic bronchitis with acute or subacute bacterial bronchitis ..	23	12	7		2	4	1				8	2		2	2	
Chronic mucopurulent bronchitis including coexistent asthmatic bronchitis	99	10	5	5	4	6		2	1	6	41	10	3	4	3	5

**After* Van der Plas. (1951).

**The serological types of pneumococci are: 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 15, 16 ,17, 18, 19, 21, 22, 23, 29, 33, 34, 35 and 41.

TABLE II.—INCIDENCE OF *H. influenzæ* IN CASES OF ACUTE AND CHRONIC MUCOPURULENT BRONCHITIS (1928–1950)

Diagnosis	Cases	*H. influenzæ* %	*H. influenzæ* in practically pure culture %
Acute mucopurulent tracheobronchitis (bronchiolitis) ..	315	83	48
Chronic mucopurulent bronchitis including coexistent asthmatic bronchitis	363	84	50

The pneumococcus group stands next to the *H. influenzæ* group in importance. Chronic mucopurulent bronchitis associated with a pure pneumococcal infection is rare: in most cases *H. influenzæ* is found along with pneumococci. Pure pneumococcal infection is commoner in acute bronchitis. Type III and the higher types of Cooper prevail. We know of one case of chronic asthmatic bronchitis infected with pneumococcus type I without co-existent lobar pneumonia.

The Neisseria group.—In chronic bacterial mucopurulent bronchitis this group is rarely found in pure culture. In acute bronchitis, on the other hand, it may be found as the only causative organism. It never causes bronchiolitis or bronchopneumonia. We find a few cases yearly of acute bronchitis associated with the presence of meningococci.

The Klebsiella group.—We found this group exclusively in cases of chronic mucopurulent bronchitis. We do not know of the occurrence of acute bronchitis caused by this group.

The Streptococcus salivarius *group.*—We found this group in 1·3% of our cases of chronic mucopurulent bronchitis, along with *H. influenzæ*. We have never met with cases of acute bronchitis caused by this group. The high incidence mentioned in textbooks is undoubtedly caused by the faulty bacteriological technique of using unwashed sputum for cultivation.

The groups of pyogenic cocci (*Staphylococcus aureus* and β-hæmolytic streptococcus) are,

in cases of acute bronchitis, nearly always associated with co-existent virus infections (notably influenza and measles), which have a cytotoxic action on the ciliated epithelium. Histological studies show fibrinous necrotising inflammation.

Escherichia coli.—This organism is absent in acute and rare in chronic mucopurulent bronchitis. However, it appears frequently after treatment with penicillin. The pathogenicity of this group in the airways seems to be low. Very often sputa containing *E. coli* do not show a heavy leucocytic exudate.

II. Acute Bronchitis

Acute bacterial bronchitis is difficult to analyse scientifically because many cases are associated with virus infections of the respiratory tract. The explanation of this association is most probably that the respiratory viruses have a cytotoxic effect on the ciliated epithelial cells of the respiratory mucosa and in this way diminish resistance to bacterial infection (Hers, 1955). In the laboratory the viruses of the influenza group (A, B and C) can easily be handled. The same holds true for the new A.P.C.—or A.R.D.—viruses. Measles and coryza are more or less readily recognizable clinically, as is the primary atypical pneumonia associated with cold-hæmagglutination.

Secondary bacterial invaders are well known in influenza and measles, much less so in coryza and still less in the diseases caused by viruses of the A.P.C. group. The existence of primary acute bacterial infections of the bronchial mucosa is doubtful, though there are indications that the groups of *H. influenzæ*, pneumococci and Neisseriæ may be primarily pathogenic (Hers and Mulder, 1953). It is certain that patients with pre-existing allergic (asthmatic) bronchitis are more susceptible than others to acute bacterial bronchitis. Primary bacterial bronchitis may develop in cases of typhoid fever, myocardial infarction and other conditions, and also as a terminal illness.

For the treatment of moderate to severe bacterial bronchitis antibiotics should be used, the choice of antibiotic depending upon the results of bacteriological examination of the sputum. In this way the process can be stopped immediately. In children the bacterial ætiology of a bronchial or bronchopneumonic process sometimes can be ascertained by examination of the purulent nasal discharge which may be associated with the bronchial process. The same holds true for cases of acute sinusitis and otitis.

Acute mucopurulent bronchiolitis (Laennec's *catarrhe suffoquant*). This disease, according to our experience, is always caused by *H. influenzæ* infection. Pneumonic consolidations of any extent are lacking in these cases (*H. influenzæ* pneumonia of the American textbooks does not exist, or is exceedingly rare). The disease is sometimes very severe and may be fatal. Adequate antibiotic treatment may be life-saving.

Transition from acute to recurring and chronic mucopurulent bronchitis.—The mechanism by which an acute bronchitis becomes chronic is still unknown. Working hypotheses are: (1) The acute bacterial bronchitis may be associated with acute sinusitis. The latter may become chronic, causing recurring bronchitis by aspiration of pathogens (about 40% of all cases of chronic mucopurulent sinusitis are associated with *H. influenzæ* infection); (2) acute bacterial bronchitis may cause persistent anatomical damage to the bronchial mucosa, e.g. multiple stenosis (Hers, 1956), which may initiate relapses or recurrences of bacterial bronchitis originating from chronic bacterial foci in the bronchi or by aerogenic reinfection; (3) acute bacterial bronchitis in predisposed individuals may initiate allergic bronchitis, which, in turn, predisposes to recurring bacterial infections.

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Professor C. H. Stuart-Harris (University Department of Medicine, Sheffield):

Field Studies in Relation to Chronic Bronchitis

Study of the causation of a long-continued process such as chronic bronchitis presents peculiar difficulties. The end of the road is a very long way away in terms of years from the beginning of the journey and mortality itself is not necessarily bound to reveal the important circumstances which played upon the patient's respiratory tract at the initiation of his disorder. Perhaps it is this very feeling of insecurity at the many deductions made so far as

a result of a study of mortality which is responsible for a revived interest in morbidity. But, in the case of all chronic disorders, morbidity studies of an epidemiological character cannot be begun unless the diagnosis of the condition is certain. Granted a physical sign, then one can begin to make progress.

Probably there would be a considerable measure of agreement amongst a group of clinicians if they were confronted with a series of patients with advanced chronic bronchitis and emphysema. But one could prophesy an equal measure of disagreement if patients in all stages of the process were assembled and diluted by the presence of an equal number of perfectly healthy persons. The truth is that whereas it is reasonable to ask a clinician to confirm a diagnosis of chronic bronchitis, it is much more difficult to say that a person does not have this condition. Two circumstances appear to be responsible for this difficulty in definition. First of all, in chronic bronchitis, symptoms are much more in evidence than physical signs, and, secondly, chronic bronchitis is particularly common after middle life, and there is a tendency for an alteration of the pattern of acute respiratory infection as one ages, so that colds have a greater tendency to lead to complications. Moreover, dyspnœa is an inevitable accompaniment of the decreasing respiratory function which sets in after 40 and is accentuated by other factors, such as obesity or a more sedentary existence.

The proposition therefore that one should begin to tackle the epidemiology of bronchitis by defining the prevalence of bronchitis in different persons living under different social and environmental circumstances is far from easy. A pilot study which was made in 1951 at an engineering and chemical industrial firm near Sheffield (Stuart-Harris, 1954) served as a clear illustration of the problem. Using symptoms alone, it was possible to correlate age with the prevalence of a history of cough and expectoration which was either persistent or only experienced at intervals, for instance during colds. The addition of dyspnœa of a defined degree to the presence of a persistent daily cough and sputum gave a rather sharper picture similarly correlated with age. The same population surveyed by the combination of physical examination, X-rays and function tests could be subdivided into 3 groups—the healthy, those with organic disease and those with indeterminate findings. The clinical diagnosis in the organically abnormal men showed a complicated mixture of heart and chest disease, with the presence of more than one condition in a significant number. It seemed that the clinical diagnosis of chronic bronchitis was a rather artificial separation of those with persistent cough and sputum, and a history of annual winter attacks, termed bronchitis after exclusion of other conditions of the chest. It follows that one can only obtain a really reliable idea of the prevalence of what the clinician terms chronic bronchitis in a community by the fullest of clinical examinations, to which must be added a chest X-ray and some form of pulmonary function test.

This pilot study led us to a second purely symptomatic study of several thousand workers at the same industrial plant in an endeavour to get away from pure clinical diagnosis. The aim was to subdivide the population into the simplest of symptomatic groups and to attempt to correlate the findings with a history of past illnesses, with occupational factors and with personal factors such as smoking. This second study was carried out by the questionnaire method and the answers to questions concerning respiratory symptoms enabled us to distinguish five categories of persons.

These were: A. those with no history of cough or sputum;
B. those with a dry cough but no sputum;
C. those with cough and sputum experienced only intermittently, such as during colds;
E. those with persistent daily cough and sputum, but no undue breathlessness;
G. those with persistent daily cough and sputum, with the addition of dyspnœa on exertion to a defined degree.

Categories A and B diminished in proportion with age, C remained at approximately the same level in each decade, and categories E and G increased in proportion with increasing age, particularly over the age of 40. Correlation of these symptomatic categories with past illnesses revealed the fact that almost all of those who suffered annually from attacks of bronchitis belonged to category G. Pneumonia in adult life and pleurisy also showed a higher incidence in category G, whereas childhood pneumonia, whooping cough, and nasal symptoms suggestive of sinusitis were not significantly correlated with any category.

It is not my purpose to detail the other results of this survey, which has revealed quite clearly, to my mind, the possibility of obtaining excellent descriptive details of a population by a very simple method. I would however like to refer briefly to the results of a similar study carried out by Dr. Marjorie Clifton, who effected much of the earlier study and who has surveyed a rural population in the North of England. Subdivision of the men over 30 in

Dr. W. N. Pickles' practice in Wensleydale gave results which contrasted with those obtained in Sheffield. The category of persistent cough and sputum without dyspnœa was less clearly correlated with age in this group. There were many fewer men with the three symptoms of persistent cough, sputum and dyspnœa in Wensleydale, but the percentage increased sharply in those over the age of 60. This rural study brought out a new occupational syndrome—new, that is, to those of us who work in towns. Working with hay, particularly at certain seasons of the year, evokes cough, sneezing and dyspnœa in some farmers, and this perhaps is a hazard due to atmospheric pollution not normally visualized by those of us who are obsessed by smoke.

Comparison of the Wensleydale and Sheffield surveys clearly shows the difficulty which exists in establishing a difference in the patterns of symptoms in different populations and then in attempting to relate these to particular circumstances, such as environment or occupation. No two populations are the same even in age and sex structure, and when one attempts to allow for the differences imposed by personal habits, occupation and all that comes under the heading of social conditions, it is practically impossible to evaluate the influence of one specific circumstance such as, for instance, the question of atmospheric pollution.

The working-party of the Medical Research Council's Sub-Committee on Chronic Bronchitis has held many meetings during the past eighteen months in order to seek to guide a programme of research. So little was known about field conditions at first that the results of various field studies now in progress were awaited. We were at first confronted with the difficulties in definition, and we have not been able to arrive at a definition which will obviate the necessity for full clinical examination, including the use of radiography. More recently we have examined the problem of establishing the significance of a reduction in atmospheric pollution, such as may be effected by the efforts of local authorities in the light of the Beaver Report and the Clean Air Bill. It will be very costly in terms of medical man-power to establish prevalence data in different areas where atmospheric pollution already exists to a different extent. Moreover, this information can only be related to past exposure to pollution, and several surveys in the same towns would have to be made if the effect of changes in pollution in the future were to be determined.

An alternative suggestion is that, by means either of surveys or through medical practitioners, panels of chronic bronchitic persons would be established in a number of different towns with different pollution levels. Such individuals would record their experience in terms of health and particularly of attacks of bronchitis. Simultaneously, records of the atmosphere would be kept in order to establish the effect of such measures as might be taken in cleaning up the smoke content of the air. It is not, of course, generally realized that records of pollution as kept at present are totally inadequate for such a detailed experiment as that now visualized. There are great differences over short distances in the actual intensity of pollution, and a large number of sampling stations would have to be set up. Moreover, in large towns or conurbations, a gradual spread of smoke-cleared areas would not produce a sharp enough change in pollution for any short-term study of the clinical effects. Smaller towns, say of 50,000 to 200,000 persons, and ones in which a vigorous attempt at a reduction of pollution could be applied, would be much more suitable.

In these areas where pollution was being reduced, it is probable that other indices such as the vital statistics, sickness absences from industry and even school absences might show a difference and must therefore also be studied. Nor is there any reason for exclusion of the elaborate clinical survey of the type referred to as a prevalence survey. This might also be effected in a few likely areas.

Other Causative Factors

Atmospheric pollution, however, is only one of the probable causative factors of chronic bronchitis. The striking correlation between bronchitis mortality and social class indicates a distinction between the incidence in Classes I and V which must be a reflection of much more than pollution. In any future programme of research there is much to be done in the elucidation of personal factors as well as of environmental ones. There is the question of heredity, of childhood infections and of habits such as smoking. There is the influence of occupation. The latter is a particularly difficult subject to investigate because of the way in which factors are linked. Thus heavy work is often dusty or dirty and it is difficult to select jobs which are heavy and not subject to any atmospheric conditions. Then again, personal factors may be linked with environmental ones—such as, for instance, heavy smoking and occupation. There seems no other way to pursue the matter than to obtain data from as many subjects in as many walks of life as possible. Climate also requires attention and it may well prove desirable to pursue parallel studies in this and other countries. Finally,

I do not feel that we can afford to neglect the detailed study of relatively few persons at different phases of the natural history of bronchitis. The so-called acute exacerbation is still somewhat mysterious. Undoubtedly many attacks are precipitated by infection but I personally favour the view that a deeper knowledge of the various respiratory viruses is required before we shall be able to understand the relative importance of bacteria such as *Hæmophilus influenzæ* in regard to acute episodes. I am still extremely dubious of the significance of the eosinophil cells in the sputum in chronic bronchitis, but, no doubt, studies such as those of Professor Mulder and his associates will, in due course, provide the answer.

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Dr. Horace Joules (Central Middlesex Hospital, London):

The extent of the problem can be measured only partially by statistics, but in 1951 bronchitis was responsible for the certified loss of 26·6 million days among the insured population, while nearly 37,000 people died of the condition (Table I). The introduction

TABLE I.—DAYS OF INCAPACITY FROM BRONCHITIS IN ENGLAND AND WALES, TOGETHER WITH TOTAL DEATHS FROM THIS CONDITION 1951

Males: Days of incapacity	20·4 million
Females: Days of incapacity	6·2 million
Males 10% of days of incapacity	
Females 6% of days of incapacity	
Total deaths	36,985

of sulphonamides, penicillin and other antibiotics has done little to affect the mortality figures. Study of the social class incidence reveals a mortality in both sexes which is five times as great in social class V as in social class I (Fig. 1). The variation in mortality in

FIG. 1.—Standardized mortality ratio for bronchitis, men and women in England and Wales 1950.

comparatively young men is equally striking when different urban areas are compared. Table II shows that Salford has a mortality for men aged 45–64 which is six times as heavy

TABLE II.—DEATHS FROM BRONCHITIS PER 100,000 IN MALES AGED 45–64 YEARS, 1950–1952

Warrington ..	321	Hastings	51
Salford	319	Eastbourne ..	63
Oldham ..	302	Gt. Yarmouth ..	67
Dudley	299	Canterbury ..	74
		Coventry	80

as that of Hastings. Several factors are responsible for this, but housing and atmospheric pollution are extremely important. Fig. 2 is taken from a photograph supplied by Dr. J. L. Burn, the Medical Officer of Health of Salford, and shows something of the condition in

FIG. 2.—Photograph of ward in Salford 1955 where bronchitis morbidity and mortality are almost the highest in the country.

a ward of the city where bronchitis mortality and morbidity are highest. Despite much effort, atmospheric pollution from sulphur gases is getting worse in that city, while pollution from solid matter is falling. This is the tendency too in London, where fogs are becoming increasingly lethal. Surely an explanation can be found here in the increasing amount of coal burnt in the centre of our city by the great electricity and gas-producing plants. In a few years there was an increase of five million tons per annum in the coal used for these purposes within the London civil defence area. The Clean Air Bill will do little to abolish this menace, for it is aimed chiefly at the household grate, which contributes less than 10% of the sulphur in the atmosphere in many highly polluted areas.

The effect of smoking on initiating and maintaining chronic cough is slowly being realized. The tremendous increase of cigarette addiction revealed by a recent controlled investigation into the habits of those with chronic bronchitis showed that the majority had smoked more than twenty cigarettes a day for more than twenty years.

The life-history of the patient with severe bronchitis is one of the most pathetic stories in human ill-health. Years of increasing pulmonary insufficiency are punctuated by recurring bouts of "pneumonia" and "asthma", with sleepless nights and a cough which distends still further the emphysematous lungs.

One of my patients fell in the street on his way home from work in the fog of 1952. He was unable to climb the stairs to bed. He slept by the fire kneeling into an easy chair. Only in this way has he been able to sleep on many foggy nights since that time.

Bronchitis presents us with a challenge and also with opportunities in preventive medicine which we shall do well to seize in the next few years.