Chronic Bronchitis

AN *NAPT* SYMPOSIUM

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Report of a meeting
held in London,
12th December 1956

NATIONAL ASSOCIATION
for the PREVENTION of TUBERCULOSIS
AND DISEASES OF THE CHEST AND HEART
Tavistock House North, Tavistock Square, London, W.C.1
65, Castle Street, Edinburgh 2
28, Bedford Street, Belfast
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Preface

Chronic bronchitis, which causes 30,000 deaths a year in England and Wales and disables thousands more, is a malady which the modern chest physician regards seriously. The *NAPT* thought it would be helpful to arrange an occasion when present-day views could be presented briefly to an audience of doctors specially interested in chest disease. The ten leading authorities who, under the chairmanship of Dr. J. L. Livingstone, contributed to this symposium, were asked to occupy no more than fifteen minutes, and to deal as far as possible with those aspects about which progress can be expected.

These articles are now presented as an authoritative survey of contemporary opinion, but it should be emphasised that they are necessarily very much compressed in form.

It is to be hoped that greater attention to this distressing condition will produce great improvements in its management.

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CHRONIC BRONCHITIS
—an *NAPT* Symposium

The Chairman's Opening Remarks

J. L. LIVINGSTONE, MD, FRCP
Physician, King's College Hospital and Brompton Hospital, Member of Council, NAPT

It gives me great pleasure, on behalf of the *NAPT*, to welcome you here today. During the last few months the *NAPT* has changed its charter to include interest in non-tuberculous disease of the lung, and in heart disease. We have done this not because we think tuberculosis is finished with—it is still a very active disease, particularly in the Colonial Territories. The work is still going on, but we do feel our interest should be turned a little more towards the non-tuberculous aspect of chest disease and so we have arranged this meeting on our old enemy bronchitis.

We have a very good programme of excellent speakers. Our time is limited and in order to cover as many aspects of the problem as possible we will have to compress a great deal into a short time.

INTRODUCTORY ADDRESS

Neville C. Oswald, MD, TD, FRCP

Diseases deserve to be studied in proportion to their importance to the health of the nation. Unfortunately, academic studies of bronchitis in the past have been few, although in recent years, probably in part because of the decline in respiratory tuberculosis, there has been an awakening of interest. The difficulties confronting anyone trying to make a significant contribution are formidable and this is bound to be so in a chronic disease of which the cause is unknown. Also, techniques of investigation have become so complex that investigators must do much preliminary work before any aspect of the disease can be tackled.

In introducing this symposium, I feel I should point out some of the problems associated with bronchitis, many of which, as yet, await investigation.

National morbidity and mortality rates, which take little account of diagnostic accuracy, supply much useful information in relation to the distribution of bronchitis by regions, occupations, age and sex. These form the basis of more detailed studies of aetiology, which show specifically where and when the disease occurs and open the way for assessment of the parts played by infection and atmospheric pollution. The recent development of statistical methods has meant that much more reliance can now be placed upon the conclusions from such surveys. These surveys are not ends in themselves, although they often supply useful pointers, especially in relation to prophylaxis ; their main purpose is to indicate which lines of investigation are likely to be fruitful.

The bacteriology seems now to be fairly well defined ; *Haemophilus influenzae* and pneumococci probably represent the most important pathogens, at least in the

later stages of the disease. The influence of viruses is virtually unknown. Virology is a new science, extending back to about 1930. It relies for the most part upon immunity reactions, animal passage, tissue culture and electron-microscopy and has yet to be seriously applied to the study of bronchitis. Experience over the past twenty years with the influenza group has led to the development of a vaccine which probably reduces the number of attacks of influenza in the vaccinated by about 40 per cent. To this extent, it is of value to bronchitics. The development of tissue culture on monkey kidneys and *Hela* cells has resulted in the isolation of a vast number of viruses from the respiratory tract, the majority of which have not yet been identified and whose pathogenicity is uncertain. Polio-, Coxsackie and adenoviruses and the enteric cytopathogenic human orphan group have now been systematically typed and the majority of these are capable of producing respiratory infection. Whether they are capable of sensitising bronchial epithelium to further infections is not known. The identification of latent viruses in the epithelium of the upper respiratory tract suggests that viruses may play an important part in the early stages of bronchitis. There is now good evidence that viruses can persist in cells after clinical infection is over and that they can be induced to multiply after several weeks of incubation in tissue culture. If it is assumed that potentially pathogenic viruses exist in a latent form in the bronchial epithelium of chronic bronchitics, they may be contributing to the chronicity of the disease.

Recent investigations of the minute pathology of bronchitis lend support to the importance of infection and should soon be able to tell us more of the relationship between bronchitis and emphysema. They also serve to emphasise the extreme importance of the mode of development of epithelial cells. If only we were able, in chronic

bronchitis, to prevent the excessive formation of goblet cells, the amount of respiratory disease in Britain would be reduced by one half.

Physiological studies which previously have been concerned to a large extent with the mechanics of emphysema can now give accurate assessments of respiratory function.

Future studies upon respiratory mucus are likely to be long and arduous, but may in the end produce the most useful information in relation to treatment. The isolation of a specific muco-protein in normal urine which inhibits the agglutination of chickens' red blood cells by influenza virus, and the subsequent identification of the carbohydrate which is split off by the virus, suggests the type of fruitful investigation which may result from combining biochemistry with immunology. Further studies of the resistance-lowering effect of mucus are overdue, especially as it is now known that bodies immune both to bacteria and viruses exist in the secretions of the respiratory tract.

Radiology, which is at the same time the most and the least helpful investigation, serves to distinguish many other diseases from bronchitis, but is often unable to distinguish between a normal chest and one with severe bronchitis and emphysema. There is room for much improvement here in the delineation of small pulmonary foci.

Clinical studies still have their place. Some bronchitics have only a mucoid sputum, some have mucus in remissions and pus in attacks, and some have pus all the time. I think that this range of reactions is most likely to be due to inherent qualities in individual lungs, but the influence of infection in determining which pattern develops remains obscure. Treatment continues to be most unsatisfactory. Once a bronchitic starts to become disabled, irreversible changes are likely to have taken place, although much symptomatic relief can often be

obtained by prophylactic means, that is, by avoiding further infection, atmospheric pollutants and adverse climate. But it is common knowledge that if these irritants can be avoided for a time, the old symptoms recur on further exposure.

Specific treatment resolves itself into three main types, namely the alleviation of the triad of excessive mucus, mucosal oedema and bronchospasm, antibiotics to combat infection and remedial exercises to enable respiration to be maintained with the least conscious effort. The least satisfactory of these is probably the first since no effective means exist for controlling mucus. Whether this will ever be accomplished seems doubtful in the present state of knowledge ; if it is, then it may well come from a combined study of biochemistry, immunology and microbiology.

The supply and demand of in-patient accommodation for bronchitics is a complex matter. Accommodation near patients' homes must be provided for acute exacerbations, and this is usually the responsibility of the general physician. Most bronchitics are prepared to come into hospital for review for three weeks during which the antibiotic and antispasmodic aspects of their bronchitis can be studied and suitable treatment indicated. Whether there is a place for bronchitics in vacant sanatorium beds has by no means been decided. It seems that some sanatoria are admitting such patients for two or three months, and the results of such arrangements urgently need to be correlated. For long-term institutional care, there is a group of elderly bronchitics, especially widowers, who are willing to enter settlements with hospital facilities when they are unable to make adequate provision on their own.

MORBID ANATOMY

Lynne Reid, MRCP, MRACP,

Research Fellow,
Institute of Diseases of the Chest, Brompton Hospital.

In describing the pathological changes in the lung in chronic bronchitis, it is convenient to consider first the changes in the bronchi, and then those which occur in the bronchioles and alveoli. The bronchi focus attention on the increased production of mucus, which is one of the earliest and most constant clinical features of the condition. In the later stages of the disease there is progressive impairment of pulmonary function and additional pathological changes in the lung periphery.

In the lung mucus is secreted by glands and goblet cells. The mucous glands are confined to the wall of the bronchi. These, by definition, are the air tubes proximal to the level at which the cartilage disappears, while the bronchioles lie distal to this point. In the normal human lung about 100 cc. of secretion are formed in twenty-four hours, but it is not known what increase is necessary for the production of mucoid sputum, which is one of the first clinical signs of chronic bronchitis. In a mild case of chronic bronchitis the production of sputum may not be associated with any visible abnormality in the bronchial epithelium, but in the well-established case it is usually reflected by an increase in the number of cells which give a positive stain for mucus.

The cilia of the bronchial epithelium are related functionally and anatomically to the goblet cells. Although, in an acute infection, they may be destroyed, cilia morphologically normal are usually still present in chronic bronchitis, but there are two ways in which their function may be disturbed. First, the effective ciliary area

of the bronchial wall may be reduced if a large number of goblet cells are discharging mucus, and, secondly, alteration in the composition of the secretion may interfere with their function. The secretion in the normal bronchial tree probably lies in two layers, a thick sticky one resting on the tips of the cilia and a deeper, more serous layer, in which the cilia beat.

An increase in the number of cells producing mucus may be the only change seen in the wall of the bronchi, but there may also be changes of acute inflammation, oedema, dilatation of capillaries and infiltration with inflammatory cells. The epithelium may be destroyed, but considerable inflammation may be present without ulceration. It is in the periphery of the lung, however, that infection causes its worst damage and permanent interference with pulmonary function.

The changes which may be present in the bronchioles include hypertrophy of the goblet cells, purulent bronchiolitis, fibrous narrowing of the lumen even to the point of obliteration, the formation of abscesses of microscopic size and dilatation.

The changes seen in the alveoli include acute pneumonia, organisation of exudate, oedema, collapse and emphysema, or pus and mucus lying in the alveolar spaces. Thus there is no lesion which can be considered specific of chronic bronchitis. Its characteristic feature seems to be the progressive involvement of the lung periphery by recurrent incidence of infection, or obstruction by secretion, or both.

Some of the inflammatory changes, such as abscess formation or pneumonic consolidation are acute, and, therefore, may resolve ; others are chronic and will not resolve. Even if acute inflammation subsides, however, any ulceration of the alveolar walls which may have occurred will remain. Thus there is loss of anatomical integrity of the bronchiole-alveolar junction, thereby

conferring the structure of a flap valve on the wall of the bronchiole.

It is a characteristic of chronic bronchitis that both at lobar and lobular levels the changes are irregular. In adjacent lobules a range of changes may be seen including emphysema, bronchiolectasis, bronchiolar obliteration and condensation of the lung into small scars. These small nodular scars are a characteristic feature of the lung periphery of many patients with chronic bronchitis. They may be deep in the lung and feel like cherry stones on palpation or in the subpleural region where they may be more plaquelike. To complicate the picture further these direct effects of the bronchitis may cause compensatory changes in neighbouring lobules.

These various lesions inevitably cause disruption of the lung capillary bed ; this is an important aspect of the disease. The pulmonary capillary bed may be reduced, by ulceration or by condensation of the alveolar walls into nodules. As the bronchioles are also involved there will be a disturbance of the capillary bed supplied by the bronchial artery. By contrast, infection may cause dilatation and increased blood flow in the bronchial artery system. This disturbs the dynamic relation between the pulmonary artery and vein and the bronchial artery and is probably one factor in the development of cor pulmonale.

Discussion of chronic bronchitis almost inevitably involves mention of emphysema. This is difficult to define, since the word means something different to the clinician, the radiologist, the physiologist and pathologist, largely because of their different techniques in examination. The pathologist, for example, can detect emphysema in a primary lobule by using a microscope, while the radiologist can only detect local emphysema if it is gross enough to affect the radiograph, or diffuse enough to cause secondary changes in the diaphragm and blood

vessels. It is unnecessary to analyse the different significations of the word to realise that the variety of changes which cause disruption of the respiratory or peripheral part of the lung are responsible for the symptom of shortness of breath. Individual lesions may be insignificant, but in total they are responsible for the severity of the disease and for the inexorable course it so often runs.

While knowledge of the changes in the lung periphery throws light on the natural history of chronic bronchitis and its various clinical features, it is the study of mucus which has drawn attention to the early stages of the disease, and presents us with the crucial problem of the initial onset.

The illustrations to this article appear facing pages 14 and 15.

INFECTION IN THE AETIOLOGY OF BRONCHITIS

J. Robert May, BA, MD,

Senior Lecturer in Bacteriology,
Institute of Diseases of the Chest, Brompton Hospital.

The title of this paper implies the part played by infection in the change from a perfectly normal healthy individual to one with established bronchitis. At present, apart from speculation, we have no clear-cut facts to help us assess the role of infection from this point of view. It is true that many bronchitics date the onset of their disability from some infective episode such as pneumonia, but whether or not the bronchitis results from the infection *per se*, or from other disturbances, it is impossible to say. I think an extensive and involved clinical trial would be necessary before one could come to any hard and fast conclusions.

In discussing infection in chronic bronchitis, it is very important to distinguish clearly between bacterial and viral infection, and I would like first to consider the bacterial element. Present information is based upon the study of subjects whose bronchitis is well established, and the importance of bacterial infection in these patients is not difficult to determine. The patients can best be considered in two groups : those with pus in their sputum and those with no pus, pus being taken as the outward and visible sign of bacterial infection. If suitable chemotherapy is given to a chronic bronchitic with purulent sputum, the sputum seldom disappears completely ; at best the pus disappears, the sputum is perhaps diminished in volume and the patient's general health may improve considerably, but chemotherapy will have no effect on the residual mucoid sputum. In contrast a patient whose sputum never contains pus will derive no benefit from