Thorax 1984;**39**:81–85

Editorial

Definitions of emphysema, chronic bronchitis, asthma, and airflow obstruction: 25 years on from the Ciba symposium

Before the publication in *Thorax* in 1959 of the report of a Ciba guest symposium,[1] international confusion about the use of the words asthma, chronic bronchitis, and emphysema was profound, but it was subsequently much lessened by three of the main proposals that emerged.

The first was that emphysema should be defined in terms of morbid anatomy. Although the proposed definition, "increase beyond the normal in the size of airspaces distal to the terminal bronchiole either from dilatation or from destruction of their walls," was subsequently modified in a report from the World Health Organisation[2] to include only lungs where there was destruction of the walls of the distal airspaces, the idea of defining emphysema in anatomical terms has been universally accepted. This transferred responsibility for the diagnosis from clinicians to pathologists; the residual problem is to convert the clear definition into quantitative criteria that can be generally accepted by pathologists.[3]

The second proposal was that chronic bronchitis should be defined as "chronic or recurrent excessive mucous secretion in the bronchial tree," diagnosed clinically by the presence of cough with expectoration that is not attributable to other lung diseases. This definition has also been internationally accepted by epidemiologists but many British clinicians have continued to use it in a wider sense, to which we present our objections later.

The third important recommendation was to introduce the concept of "airflow obstruction," previously absent from clinical terminology. The term generalised obstructive lung disease (GOLD) was used to include both reversible (or intermittent) obstruction and irreversible (or persistent) obstruction. This led to a definition of asthma in functional terms which has been widely accepted in principle, but the difficulty of defining a threshold of reversibility above which asthma should be diagnosed remains despite a further Ciba study group report in 1971[4] and much debate. Where reversibility is virtually complete and there is evidence of an allergic or immunological basis the diagnosis of asthma is clear. But clinicians also recognise that individuals who initially have reversible obstruction commonly develop persistent airflow obstruction later in life (pp136–41).[4a] Though such individuals can often be identified by their past history or the presence of atopy, nasal symptoms, or eosinophilia, nothing is known about the cause and site of this type of irreversible airflow obstruction and this requires further study.

The Ciba term generalised obstructive lung disease has never come into widespread use, largely because a closely related term, chronic obstructive pulmonary disease (COPD), was introduced in North America shortly afterwards to refer to patients without atopy and with minimal reversibility. The word irreversible was seldom used because most individuals with mainly irreversible obstruction show some improvement after bronchodilator or corticosteroid treatment.

Before the Ciba symposium clinicians freely diagnosed emphysema when a patient with chronic expectoration became persistently breathless on exertion; the mechanical effect of coughing was blamed without any mention of smoking.[5] Nevertheless, occasional patients were described whose breathlessness had been studied in great detail in life but who proved to have no emphysema at postmortem examination.[6,7] The perplexity of British clinicians faced at necropsy with such a patient without any emphysema was revealed in a clinicopathological conference held under the title "Emphysema" at the Postgraduate Medical School in London in 1951.[7] The pathologist, Dr CV Harrison, made a diagnosis of "chronic bronchiolitis," a proposal to which we shall return. After the Ciba symposium several studies in the United States and the United Kingdom assessed the amount of emphysema in patients with severe airflow obstruction by a variety of clinical, radiological, and physiological criteria

Address for reprint requests: Dr NB Pride, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS.

and subsequently by clinicopathological correlations. The amount of emphysema ranged from zero to almost total lung destruction in patients with similar severity of airways obstruction, which led to the concept of distinctive bronchial and emphysematous types of chronic airways obstruction.[8]

Although expectoration tended to be more profuse in patients with the bronchial type of obstruction, at this time the site and nature of the bronchial or bronchiolar disease responsible for the obstruction to airflow were uncertain. Most pathological studies in the non-emphysematous cases concentrated on the large bronchi, although occasional cases were described in which obstruction was attributed to bronchiolar stenoses.[9] The recognition of the bronchial type of patient represented a radical change in clinical thinking in the United Kingdom. Emphysema was diagnosed more cautiously and more attention was paid to phlegm production. Pathologists had concluded from the close anatomical association that peripheral bronchial infection caused emphysema.[10 11] In the presence of mucous hypersecretion the sterility of the bronchi was lost,[12 13] so it was reasonably assumed that while chronic bronchitis could sometimes be a trivial symptom, as the Americans had always regarded it, it could also be a precursor of infections that could damage either the bronchi or the alveoli, causing the two contrasting types of airflow obstruction.

This concept was accepted by the Bronchitis Research Committee of the Medical Research Council (MRC). Reporting on the definition and classification of chronic bronchitis in 1965,[14] it recommended division into (*a*) simple chronic bronchitis with chronic or recurrent mucoid hypersecretion sufficient to cause expectoration; (*b*) chronic or recurrent mucopurulent bronchitis when the sputum was persistently or intermittently mucopurulent; and (*c*) chronic obstructive bronchitis when chronic bronchitis was associated with persistent, widespread narrowing of the intrapulmonary airways. Though this report was much less comprehensive than that of the Ciba guest symposium, it established, at least in Britain, the term chronic obstructive bronchitis, which emphasised that when chronic bronchitis was associated with obstruction this was not necessarily due to associated emphysema. Unfortunately, it may have promoted a view about the irreversible airflow obstruction of smokers that is now known to be wrong: namely, that the simple, purulent, and obstructive forms of bronchitis (with or without emphysema) represent steps in a causal chain that constitute its natural history—hypersecretion encouraging bronchial infection, which in turn damages the bronchi or alveoli and leads to impairment of airflow. This theory was first disproved by a prospective study in West London,[15] which showed that neither chronic expectoration nor the associated bronchial infection was causally related to the development of airflow obstruction, but that both were relatively independent responses to cigarette smoke and were associated with each other only because of the common factor of smoking. Subsequently this conclusion has been confirmed by a French prospective study[16] and by an analysis of causes of death in a 20–25 year follow up of 2718 men who had originally had measurements of FEV_1 and questionnaires on hypersecretion of mucus.[17] These studies reduced the role of chronic bronchitis to that which had been accepted before the 1950s; for, while individuals with chronic expectoration were liable to recurrent episodes of purulent bronchitis with time off work, these infections were found to have no detectable effect on disability and prognosis, except when an acute infection precipitated dangerous respiratory failure in a patient who already had severe airflow obstruction.

At the time of the MRC report on chronic bronchitis no physiological methods were available to define the precise site of obstruction to airflow, but Reid[18] had already established that the major site of mucous gland hypertrophy was in the large bronchi. The introduction of the retrograde catheter technique in the late 1960s enabled Hogg *et al*[19] to measure airways resistance and its central and peripheral components in lungs at necropsy. They showed that the dominant site of irreversible airflow obstruction due to primary airway disease lay in the peripheral airways of less than about 3 mm diameter. This important result has been confirmed by two subsequent studies.[20 21] Hence the major sites of obstruction and hypersecretion appeared to be in different sized airways, a finding which supported the epidemiological evidence for distinguishing the hypersecretory and the obstructive components of bronchial (and bronchiolar) disease and confirmed that the term chronic obstructive bronchitis is misleading.

Several pathological studies in the 1950s[10 11 22] had established that bronchiolar changes were frequently found in association with emphysema—indeed this association had been observed by Laennec.[23] The new physiological studies emphasised the need to quantify these changes. This has proved very difficult because of the enormous numbers of peripheral airways and the large increases in resistance found with relatively subtle narrowing or local stenoses when many parallel airways are affected.[24] The most specific change is goblet cell metaplasia, which can cause mucus plugging and may displace the surface layer of surfactant, allowing the airways to close more easily. The airways may also be

blocked by inflammatory exudate and become distorted, stenosed, and even obliterated. All these changes are often found in association with emphysema, but are also present in the lungs of patients who have died of airflow obstruction without emphysema, when they are presumably the main cause of the obstruction. The lesions may be distributed patchily along the length of the peripheral airways and so are easily missed in a few random histological sections. Presumably this accounts for the failure of earlier authors (including ourselves) to observe these lesions either at the time of death or on subsequent review of the available sections. The term which the Montreal group originally suggested to describe these changes was "small airways disease," which has been widely used and has been extended to include associated abnormalities of function. The term is unsatisfactory for it does not indicate their chronicity, their obstructive effect, or their pathogenesis. Even the location is loosely defined. One of the originators of the term now considers that it "has become so ambiguous as to have become almost meaningless."[24]

Although studies of lungs at postmortem examination consistently show that the major site of increased resistance is in the peripheral airways, in life the results of tests of large airway function are also often abnormal even in young smokers with only mild airway disease.[25-27] A plausible explanation for this discrepancy is that there is an additional component of narrowing in life due to increases in bronchial muscle tone or swelling of the bronchial mucosa that chiefly affects the larger airways. This would be compatible with the "Dutch hypothesis"[28] that smokers with progressive airflow obstruction show increased bronchial reactivity and atopic features similar to, but less pronounced than, those found in subjects with asthma. Recent studies confirm that some allergic features are more common in smokers[29] and that bronchial reactivity to inhaled histamine is increased.[30,31] Reduction in "reactive" large airway narrowing might explain why bronchodilators usually improve airways conductance more than forced expiration values.[32] Similarly "reactive" changes could explain why airway function is reduced for several weeks after acute infections in patients with chronic airflow obstruction[33,34]; this time course resembles that of the increased bronchial reactivity in normal people after viral infections.[35] Hence, while the major and irreversible component of non-emphysematous airflow obstruction in smokers may be located predominantly in the peripheral airways, a lesser and partly reversible component may affect larger airways.

Despite these advances, two major problems identified 25 years ago in the Ciba guest symposium persist. The first is to agree on a suitable descriptive term for non-emphysematous irrreversible airways obstruction. Two subsequent labels—chronic obstructive bronchitis and small airway disease—have serious but opposite weaknesses: the former implies a disproved pathogenetic mechanism and the latter is vague.

The second problem is to quantify the dividing line between asthma and mainly irreversible airflow obstruction. The proposal of the Ciba guest symposium was to include all subjects with obstruction in the omnibus term generalised obstructive lung disease. This was a more logical approach than that in which asthma and chronic obstructive pulmonary disease are initially separated by qualitative clinical impression. Interestingly, the only country to adopt the other omnibus term proposed by the Ciba guest symposium, chronic non-specific lung disease, was The Netherlands, which supplied the idea that the reversible airflow obstruction of asthma and the largely irreversible airflow obstruction of susceptible smokers were two aspects of the same basic process. At the time this was not a popular hypothesis in the United Kingdom and North America, where clinicians thought they had no difficulty distinguishing patients with asthma (often young, usually nonsmokers, and with clear evidence of an immunological basis) from those with mostly irreversible obstruction (usually elderly, almost always smokers). Their subsequent failure to achieve a precise definition of asthma[4] and the recent renewed interest in the Dutch concept shows how far we still have to go to reach a full understanding of the pathogenesis of the various forms of chronic airflow obstruction.

These considerations lead to the following proposals on terminology.

(1) The term *chronic bronchitis* should be used *only* to denote chronic or recurrent bronchial hypersecretion, clinically diagnosed by the presence of chronic expectoration with no other cause. The quality of the sputum may be further described as mucous, purulent, eosinophilic, etc. Such terms as "severe" or "advanced" chronic bronchitis should be used only to refer to the expectoration, not (as continues to be done in prominent British medical journals[36]) to imply the presence of associated airflow obstruction. A legitimate objection to the term bronchitis is that it implies inflammation, of which there is usually no evidence in the hypertrophied glands which produce the excess mucus. The term bronchial catarrh, originally proposed by Laennec,[23] would be more appropriate, but we doubt whether it would be accepted as a substitute for bronchitis. The definition of chronic bronchitis

proposed by a WHO committee in 1975[37] is useless since it includes all known types of bronchial disease.

(2) The term *chronic obstructive bronchitis*, implying anatomical and causal relations between hypersecretion and obstruction, should be abandoned.

(3) Where, as is common in clinical practice, the cause of persistent airflow obstruction has not been determined, simple descriptive terms should be used such as chronic airflow obstruction or limitation. The common North American term chronic obstructive pulmonary (or lung) disease is synonymous but is an unnecessary word longer. "Chronic" usefully permits a small degree of reversibility.

(4) Communication between investigators would be improved if a suitable term were adopted for the non-emphysematous irreversible obstructive disease of the peripheral airways in smokers. As already indicated, "chronic obstructive bronchitis" and "small airway disease" both appear unsuitable. "Chronic obstructive bronchiolitis" would have certain advantages, though obstructive changes probably also extend into smaller bronchi and, as with bronchitis, some of them may not be due to conventional inflammatory processes. But it is certainly preferable to the existing terminology. Obliterative bronchiolitis due to virus infections is recognised in childhood[38] and more recently "obliterative bronchiolitis" has been used to describe the peripheral airway disease found occasionally in rheumatoid arthritis and other connective tissue disorders.[39–41] In these conditions also pathological changes are not confined to the bronchioles but extend at least to small bronchi. They could readily be distinguished from the common smoking related disease by an appropriate prefix, such as viral or rheumatoid obstructive bronchiolitis.

The participants in the Ciba Symposium 25 years ago were careful to point out that their recommendations were "provisional," but it is remarkable how well they have stood up to intensive subsequent investigations. Any further modifications must also be provisional, as understanding of the pathogenesis of these conditions is incomplete. We hope that our small supplement will inhibit the use of the inappropriate term chronic obstructive bronchitis and stimulate interest in finding a more accurate alternative.

CM FLETCHER
NB PRIDE
Department of Medicine
Royal Postgraduate Medical School
London

We thank Professors Brian Heard and WM Thurlbeck for reviewing the pathology of our earlier series of patients and Professor Thurlbeck for valuable comments on this paper.

References

[1] Ciba Guest Symposium. Terminology, definitions and classifications of chronic pulmonary emphysema and related conditions. *Thorax* 1959;**14**:286–99.
[2] World Health Organisation. *Chronic cor pulmonale: report of an expert committee.* Geneva: WHO, 1961. Technical report series, No 213.
[3] Thurlbeck WM. Overview of the pathology of pulmonary emphysema in the human. In: *Emphysema. Clinics in Chest Medicine*. Philadelphia: WB Saunders (in press).
[4] Ciba Foundation Study Group No 38. *Identification of asthma* (Porter R, Birch J, eds). Edinburgh: Churchill Livingstone, 1971.
[4a] Brown PJ, Greville HW, Finucane KE. Asthma and irreversible airflow obstruction. *Thorax* 1984;**39**: 136–41.
[5] Christie RV. Emphysema of the lungs. *Br Med J* 1944;i:105–8, 143–6.
[6] Baldwin E de F, Cournand A, Richards DW jun. Pulmonary insufficiency. III—A study of 122 cases of chronic pulmonary emphysema. *Medicine (Baltimore)* 1949;**28**:201–237.
[7] Clinico-Pathological Conference, No 10. Emphysema. *Postgrad Med J* 1951;**27**:25–32
[8] Burrows B, Fletcher CM, Heard BE, Jones NL, Wootliff JS. The emphysematous and bronchial types of chronic airways obstruction. *Lancet* 1966;i:830–5.
[9] Esterly JR, Heard BE. Multiple bronchiolar stenoses in a patient with generalised airways obstruction. *Thorax* 1965;**20**:309–16.
[10] Reid LMcA. Pathology of chronic bronchitis. *Lancet* 1954;i:275–8.
[11] McLean KH. The pathogenesis of pulmonary emphysema. *Am J Med* 1958;**25**:62–74.
[12] Brumfitt W, Willoughby MLN, Bromley LL. An evaluation of sputum examination in chronic bronchitis. *Lancet* 1957;ii:1306–9.
[13] Lees AW, McNaught W. Bacteriology of lower respiratory tract secretions, sputum and upper respiratory tract secretions in "normals" and chronic bronchitics. *Lancet* 1959;ii:1112–5.
[14] Medical Research Council. Definition and classification of chronic bronchitis for clinical and epidemiological purposes. *Lancet* 1965;i:775–9.
[15] Fletcher CM, Peto R, Tinker CM, Speizer FE. *The natural history of chronic bronchitis and emphysema. An 8-year study of working men in London.* London: Oxford University Press, 1976.
[16] Kauffmann F, Drouet D, Lellouch J, Brille D. Twelve years' spirometric changes among Paris area workers. *Int J Epidem* 1979;**8**:201–12.
[17] Peto R, Speizer FE, Cochrane AL, *et al*. The relevance in adults of air-flow obstruction, but not of mucus hypersecretion, to mortality from chronic lung disease. *Am Rev Respir Dis* 1983;**128**:491–500.

[18] Reid L. Measurement of the bronchial mucous gland layer. A diagnositic yardstick in chronic bronchitis. *Thorax* 1960;**15**:132–41.

[19] Hogg JC, Macklem PT, Thurlbeck WM. Site and nature of airway obstruction in chronic obstructive lung disease. *N Engl J Med* 1968;**278**:1355–60.

[20] Silvers GW, Maisel JC, Petty TL, Filley GF, Mitchell RS. Flow limitation during forced expiration in excised human lungs. *J Appl Physiol* 1974;**36**:737–44.

[21] Van Brabant H, Cauberghs M, Verbeken E, Moerman Ph, Lauweryns JM, Van de Woestijne KP. Partitioning of pulmonary impedance in excised human and canine lungs. Functional-structural relationships. *J Appl Physiol* 1984; (in press).

[22] Spain DM, Kaufman G. Basic lesion in chronic pulmonary emphysema. *Am Rev Tuberc* 1953;**68**:24–30.

[23] Laennec RTH. A treatise on the diseases of the chest and on mediate auscultation. Trans Forbes J. 4th ed. London: Longmans, 1834.

[24] Thurlbeck WM. The anatomical pathology of chronic airflow obstruction. *Current Pneumonology* 1982;**4**: 1–24.

[25] Knudson RJ, Burrows B, Lebowitz MD. The maximal expiratory flow-volume curve: its use in the detection of ventilatory abnormalities in a population study. *Am Rev Respir Dis* 1976;**114**:871–9.

[26] Oxhøj H, Bake B, Wilhelmsen L. Ability of spirometry, flow-volume curves and the nitrogen closing volume test to detect smokers: a population study. *Scand J Resp Dis* 1977;**58**:80–96.

[27] Enjeti S, Hazelwood N, Permutt S, Menkes H, Terry P. Pulmonary function in young smokers: male-female differences. *Am Rev Respir Dis* 1978;**118**:667–76.

[28] Orie NGM, Sluiter HJ, de Vries K, Tammeling GJ, Witkop J. The host factor in bronchitis. In: *Bronchitis. An international symposium, 27–29 April 1960, University of Groningen.* Assen: Royal Van Gorcum, 1961: 43–59.

[29] Burrows B. An overview of obstructive lung diseases. *Med Clin North Am* 1981;**65**:455–71.

[30] Barter CE, Campbell AH. Relationship of constitutional factors and cigarette smoking to decrease in 1-second forced expiratory volume. *Am Rev Respir Dis* 1975;**113**:305–14.

[31] Taylor RG, Gross E, Joyce H, Holland F, Pride NB. Bronchial reactivity and rate of decline in FEV_1 in smokers and ex-smokers. *Thorax* 1983;**38**:710.

[32] Miller JM, Gall G, Sproule BJ. Work of breathing before and after bronchodilators in patients with emphysema. *Dis Chest* 1965;**48**:458–63.

[33] Smith CB, Kanner RE, Golden CA, Klauber MR, Renzetti AD jun. Effect of viral infections on pulmonary function in patients with chronic obstructive pulmonary diseases. *J Infect Dis* 1980;**141**:271–80.

[34] Tattersall SF, Benson MK, Hunter D, *et al*. The use of tests of peripheral lung function for predicting future disability from airflow obstruction in middle-aged smokers. *Am Rev Respir Dis* 1978;**118**:1035–50.

[35] Empey DW, Laitinen LA, Jacobs L, Gold WM, Nadel JA. Mechanisms of bronchial hyperreactivity in normal subjects after upper respiratory tract infection. *Am Rev Respir Dis* 1976;**113**:131–9.

[36] Anonymous. Long-term oxygen and advanced chronic bronchitis. *Lancet* 1981;i:701–2.

[37] World Health Organisation. Epidemiology of chronic non-specific respiratory diseases. *Bull WHO* 1975; **52**:251–9.

[38] Wohl MEB, Chernick V. Bronchiolitis. *Am Rev Respir Dis* 1978;**118**:759–81.

[39] Geddes DM, Corrin B, Brewerton DA, Davies RJ, Turner-Warwick M. Progressive airway obliteration in adults and its association with rheumatoid disease. *Q J Med* 1977;**46**:427–44.

[40] Epler GR, Snider GL, Gaensler EA, Cathcart ES, Fitzgerald MX, Carrington CB. Bronchiolitis and bronchitis in connective tissue diseases. *JAMA* 1979; **242**:528–32.

[41] Turton CW, Williams G, Green M. Cryptogenic obliterative bronchiolitis in adults. *Thorax* 1981; **36**:805–10.