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CONFERENCE REPORT

Precise diagnosis of airflow obstruction - does it matter for treatment?* SEPCR Workshop, Wiesbaden 1989

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CONTENTS

Some problems with current labels

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Two central problems were addressed by the Ciba symposium in the late 1950s - defining the established terms asthma, chronic bronchitis and emphysema and incorporating the presence (or absence) of intrapulmonary airways obstruction with these established labels [1]. The solutions proposed seem logical enough 30 years later, but have not been consistently adopted in clinical practice [2].

Emphysema, asthma, chronic bronchitis

From the outset it was recognized that the definitions proposed - using a mixture of morphological, physiological and clinical criteria - were provisional. The most satisfactory was for emphysema which was defined in morphological terms. Admittedly, there was an initial false start when the Ciba symposium proposed a definition which allowed *either* dilatation or destruction of the walls of peripheral airspaces, but shortly after reports from the World Health Organisation and American Thoracic Society proposed destruction as the key finding, as did the recent National Heart, Lung and Blood Institute workshop [3] which, in addition, suggested explicit excluding simple airspace enlargement (congenital or acquired) and spaces occurring with fibrosis and scarring (e.g. post tuberculosis cavities or honeycomb lung); but these conditions had not caused much practical confusion earlier. Of course, definitions can be made at a more basic level than gross morphology; in the case of homozygous alpha$_1$ protease inhibitor deficiency the specific genetic defect can be defined and the whole constellation of changes from the molecular defect through to the morphological, physiological and clinical features can then be satisfactorily encompassed in a single term. There are a few other well-defined conditions such as asthma due to specific occupational causes. But overall it has been difficult to define asthma at a more basic level than that of variable airways obstruction, although the recent claim that the diagnosis is always strongly related to a high level of total IgE in relation to age-specific levels in the population [4] may outdate previous concepts of extrinsic and intrinsic forms of asthma; others have suggested a

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morphological definition as chronic eosinophilic bronchitis. But even though no one has been able to quantify the current physiological definition satisfactorily in terms of the scale of the variation in airway narrowing required for the diagnosis of asthma, both doctors [2] and patients appear to find the term self-explanatory.

The Ciba symposium established chronic bronchitis as a clinical diagnosis for which the criterion was chronic or recurrent cough with expectoration which was not attributable to a specified list of diseases. There was no implication of associated airways obstruction. The definition proposed by the American Thoracic Society was similar but it has attracted considerable conceptual and practical criticism, although paradoxically better technical criteria using precise duration of cough have been established for making the diagnosis than for emphysema or asthma. The term implies inflammation of the bronchial wall. At the time the label was defined it was generally thought mucosal inflammation was not present in the chronic, stable state of chronic bronchitis and there were advocates of terms such as chronic mucous hypersecretion or bronchorrhoea. Shortly afterwards however inflammation was described in bronchoscopic mucosal biopsies and this has been confirmed in recent years. Clearly however mucosal inflammation could exist without hypersecretion from mucous glands.

Obstructed or not obstructed?

At a practical level, clinicians, at least in the UK, were reluctant to accept the Ciba symposium definition of chronic bronchitis and often used the term 'severe' to indicate, not copious hypersecretion or mucosal inflammation, but the presence of airways obstruction. Of course none of the three classic terms indicated the presence or absence of obstruction. Both emphysema and chronic bronchitis might or might not be associated with airways obstruction; asthma probably implies that obstruction is present at least some of the time, but this could be absent at others. The Ciba symposium proposed therefore a new term, chronic non-specific lung disease (CNSLD) for the whole spectrum of these diseases (obstructed or not). This term was adopted in The Netherlands, whose workers felt it correctly reflected their reluctance to divide this group of patients into those with and those without asthma because of overlapping pathogenetic factors, symptoms and clinical features. Most other countries continued initially to divide patients into those with and without asthma and did not use the term, which was unattractively vague. The term proposed by the Ciba symposium for the subgroup of CNSLD with airways obstruction was generalized obstructive lung disease (GOLD). The suggestion was that GOLD should be divided into a reversible condition (asthma) and an irreversible condition - the latter being defined as unaffected by bronchodilator drugs and corticosteroids over a period of more than one year. This also floundered, not on the grounds that complete irreversibility was rare, but because clinicians (outside The Netherlands) felt they could distinguish asthma without difficulty. A glance at the chapter headings of modern textbooks of medicine confirms the continuation of this confidence.

Different types of obstructive lung disease

In the early 1960s considerable efforts were made to distinguish the roles of emphysema and of intrinsic disease of the airways in impairing airway function. For example the dominant hypothesis in the UK in the 1960s was that chronic bronchitis with mucoid secretion (simple bronchitis) was important because it predisposed to recurrent bronchial infection (mucopurulent bronchitis) which in turn led to bronchial damage and obstruction (chronic obstructive bronchitis). This attempt to grade the severity of chronic bronchitis has not proved to be useful because of the subsequent recognition of the relative independence of the hypersecretory and obstructive disorders associated with smoking; furthermore the predominant site of obstruction is usually in the respiratory bronchioles and the smallest bronchi [1]. However, it was soon realized that the respective roles of emphysema and intrinsic airways disease could not be assessed accurately except at the very extremes of the spectrum when *only* airways or *only* airspaces were abnormal and so the non-descript term chronic obstructive pulmonary disease (COPD) was introduced in North America. COPD has been defined as 'a chronic, slowly progressive airways obstructive disorder resulting from some combination of pulmonary emphysema and irreversible reduction in the calibre of the small airways of the lung'. The intention was certainly to exclude asthma but no explicit criteria to do so were introduced. Hence COPD almost always fails as a short-hand label, requiring explanatory statements such as 'stable airways obstruction while on maximal conventional therapy' or 'symptomatic chronic airways obstruction, not thought to be due to asthma, which was attended by abnormalities of lung function not reversed completely by the usual therapy' to quote descriptions used for COPD patients in two recent important trials. The problem of course is that reversibility is itself difficult to define, what drugs should be used, how long should studies be made, should change be related to predicted or baseline values? This topic is discussed in detail later in this symposium.

There are other subdivision problems - what do we call the individual who starts with highly reversible and variable airflow obstruction which gradually becomes fixed and truly mainly irreversible years later? (fig. 1). Is this "persistent asthma" or just COPD? And there are large overlapping areas between asthma and COPD.

The list of conditions excluded from COPD is not entirely logical. Presumably extrathoracic airways obstruction is always excluded. By convention cystic fibrosis and bronchiectasis are excluded; so probably is byssinosis. Alpha$_1$ protease inhibitor deficiency is probably included even when the sufferer is a never-smoker but the lengthening list of specific causes of

chronic obstructive bronchiolitis (chemical injury, virus infections, graft-versus-host disease, following lung transplantation, connective tissue disorders) are excluded, although their pathology closely resembles that of the obstructive bronchiolitis found in smokers. Perhaps the common factor in exclusion is a perception that the chronic airways disease is not associated with a risk of developing emphysema.

And there is a peculiar inclusion problem, which results from the Anglo-American failure to adopt CNSLD. What do we call emphysema and chronic bronchitis without airflow obstruction? SNIDER [5] has proposed a definition of COPD in which airflow obstruction need not be present at all times during the process to solve this problem. The title of our recent paper on diagnostic labels [2] referred to chronic airflow obstruction although one of the model cases had no obstruction.

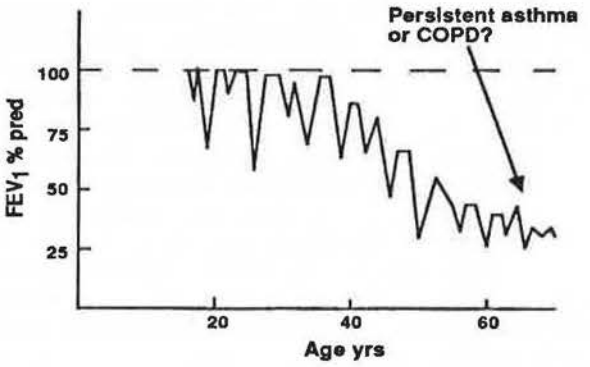

Fig. 1. – Change in functional pattern with time. Does the diagnosis change?

Are labels important?

The whole point of a label is to provide transferable information in the most economical fashion. In poorly defined conditions, confusion about the disease is reflected in confusing labels, which often are more obvious to outsiders than to those in the field who have become habituated to the problems. Whether this matters is often examined from a narrow perspective. A clinician may claim to try all treatments in all patients and ignore semantics, but poorly defined labels make it difficult to examine epidemiological trends, complicate trials of treatment, impede communication between doctors, and between doctors and patients; despite frequent assertions to the contrary by individual clinicians, overall they probably also impede correct treatment. None of us wants to be too interested in semantics but it is careless not to examine our practice periodically.

Conclusions

I have based this short review on the Ciba symposium recommendations because I think they remain the most thoughtful and structured approach, not because I think they provided a totally satisfactory answer to the problems of labelling. Many of the suggestions of the symposium were adopted, while those which were not adopted - such as the terms CNSLD and GOLD - had a logical basis, not obviously superceded by later labels.

Some suggestions on the way forward are made in the next paper. If possible, improvement should be based on more systematic use of existing labels. Although it is tempting to clear away the accumulation of past false associations by proposing new labels, they commonly add to the vocabulary (and the potential for confusion) rather than replace earlier terms.

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