Making the diagnosis of asthma

Measurement of airway responsiveness should be more readily available

EDITOR—I welcome Taylor's call for greater use of objective tests of variable airflow obstruction in patients with suspected asthma and particularly his cautious endorsement of measurement of airway responsiveness.¹ I do not, however, agree with him that the relatively weak correlation between measures of the variability in peak expiratory flow and airway responsiveness (observed in community studies) confirms that these tests measure different pathophysiological aspects of asthma. A more likely explanation is that, in most situations, both tests identify a similar abnormality but that measurement of airway responsiveness does so much more successfully than serial monitoring of peak expiratory flow.

This view is supported by several studies showing that, to achieve the same level of specificity, the sensitivity of various measures of the variability in peak expiratory flow in detecting symptomatic asthma in a community population is two to four times less than that of measurement of airway responsiveness.²⁻³ Furthermore, if attempts are made to increase the signal (and presumably the sensitivity) of variability in peak expiratory flow by incorporating readings obtained after use of a bronchodilator the correlation with measurement of airway responsiveness becomes close.⁴

In a population in which the diagnosis of asthma is in doubt the low sensitivity of measures of variability in peak expiratory flow plus the relatively high incidence of false positive and negative results due to measurement error, poor compliance, and perhaps upper airway dysfunction⁵ seriously limits its diagnostic value. Is it not time Britain followed the rest of the developed world and made measurement of airway responsiveness more readily available?

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Trial of steroids is useful

EDITOR—I am mystified why Taylor failed to discuss, or even mention, the objective response to corticosteroid treatment, which most clinicians now use to establish a diagnosis of asthma.¹ The "steroid trial" that I and most of my colleagues use is simple,

safe, and of great diagnostic help, especially in adults when the clinician is confronted by the common clinical dilemma of differentiating between asthma and chronic obstructive airways disease. Taylor correctly emphasises the value of serial measurements of peak flow in the diagnosis of asthma. He ignores, however, the even more important information obtained if one asks the patient to continue to record peak expiratory flow values twice daily while taking prednisolone 30 mg or 40 mg once daily in the mornings for 10-14 days. This, in my experience, is the most important investigation of any patient with chronic airflow obstruction.

Challenge tests with methacholine have little or no diagnostic role in clinical respiratory medicine but are used extensively by epidemiologists, who usually have great difficulty in defining the clinical relevance of positive, or even negative, results of challenge tests. Taylor refers on more than one occasion to the "bronchodilator reversibility test." His comments about the diagnostic value of such a test are vague. On balance I think he doubts the reliability of this frequently performed investigation, and if my interpretation of his views is correct he has my full agreement. It may be that Taylor is a paediatrician or epidemiologist and this is why his editorial will be little help, and indeed may create some confusion, if read by a clinician concerned primarily with adult patients with airways disease.

The steroid trial does not diagnose asthma. Nevertheless, patients with chronic airflow obstruction in whom mean peak expiratory flow improves by $\geq 15\%$ during treatment with oral prednisolone should be treated as if the primary diagnosis was asthma.

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- 1 Taylor R. Making the diagnosis of asthma. *BMJ* 1997; 315:4-5. (5 July.)

Relation between asthma and bronchial hyperresponsiveness is not clear cut

EDITOR—Taylor makes a valiant effort to grapple with the enduring problem of how you diagnose asthma.¹ He places undue emphasis, however, on tests of non-specific bronchial hyperresponsiveness. Although at a population level bronchial hyperresponsiveness is clearly related to asthma, this relation is not so clear cut at the individual level and is influenced by definitions used for asthma and bronchial hyperresponsiveness.

At any one time only two thirds of people with asthma diagnosed on the basis of symptoms show bronchial hyperresponsiveness, while one third have no current respiratory symptoms.²⁻³ Clough et al reported a longitudinal study of 196 children assessed over 12 months.⁴ Bronchial responsiveness to methacholine was tested every month and varied considerably over the course of the study: a third of the children showed a variation of more than four doubling dilutions in the cumulative

dose of methacholine resulting in a 20% fall in forced expiratory volume over the 12 months. Of those who were both atopic and reported wheeze, 11% did not have bronchial hyperresponsiveness at any time during the study. Specific tests of bronchial responsiveness may be superior to non-specific tests such as methacholine. Avital et al have shown that adenosine is a better discriminator than methacholine both between asthma and absence of bronchial disease and between asthma and other causes of chronic obstructive pulmonary disease.⁵

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- 1 Taylor DR. Making the diagnosis of asthma. *BMJ* 1997;315:4-5. (5 July.)
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Compliance is not all

EDITOR—Bamforth is correct in spotting the wrong preposition in the quotation from Franz Kafka.¹ In the course of some enthusiastic technical editing of my article, Kafka was omitted and restored only as the result of my last minute appeal on the telephone.² Somehow BT (the telecommunications company), my diction, and the technical editor's hearing conspired to substitute the offending preposition. Bamforth's summary of Kafka's story, however, usefully warns us of the contrast between professional empathy (a cornerstone of concordance) and uncontrolled transference (the fate of Kafka's fictional doctor). In the working party report that I referred to, the correct translation of Kafka's quotation appears, as Bamforth gives it.³

In their letter Milburn and Cochrane express three reservations about concordance.⁴ Firstly, they observe that drug trials demand high levels of compliance to establish effectiveness and dose. In clinical practice half of patients with chronic conditions fail to achieve this compliance. Does this mean that the results of these trials can be of help only to (an unpredictable) half of the population of patients to be treated? The single-minded pursuit of compliance may provide proof of effectiveness but seems unable to deliver reliable benefit.

Secondly, they claim that cognitive analytic psychotherapy has helped to improve patients' compliance. If as a consequence the patient is able to benefit more fully from the treatment then he or she does so as an active partner. Psychotherapy aims to empower, not control, the

patient. Surely this is an argument not for compliance but for concordance.

Thirdly, they remind us that threats to the public health (posed, in their example, by non-compliant patients with open pulmonary tuberculosis) demand nothing less than strict compliance with drug treatment, in the public interest. There are similar examples from forensic mental health. Nothing in the concept of concordance asserts the necessary primacy of individual autonomy over the needs of society.

In setting out our agenda of research, training, and public awareness, our working party was only too aware that we were not providing definitive answers to the problems caused by non-compliance in medicine taking. Rather, we wished to suggest a more productive way of asking the questions

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Assessing methodological quality of published papers

Pre-allocation bias in randomised controlled trials must be taken into account

EDITOR—In her article on assessing the methodological quality of published papers, Greenhalgh does not draw sufficient attention to one of the main sources of bias found in randomised controlled trials.¹ This can occur before the allocation procedure itself and is, therefore, easy to miss.

Recruitment to the trial usually requires that subjects accept the offer of either of two forms of treatment. In many cases, one of the treatments may be so strongly preferred to the other on a priori grounds that the offer is rejected at this stage. Since the patients' attitudes, beliefs, and expectations may affect their response to and compliance with treatment procedures, this issue has considerable importance for research into the effectiveness of treatment.

Providing full data on how many people were initially approached to generate the trial sample is a necessary requirement for any research trial, but these data are often not given. Where refusal rates are relatively high it becomes imperative to re-examine the characteristics of subjects entering the trial to ensure that these are comparable with those of the intended target group. For some of the more overt characteristics (such as age, sex, and severity of symptoms) this may be relatively straightforward. Where the factors influencing entry to the trial are covert (such as expectations about treatment) or unknown (which is often the case) the detection of this sort of pre-selection bias and the

assessment of representativeness is often complex and extremely problematic.

Randomised controlled trials are correctly seen as potentially one of the most powerful tools in research into treatment, and results from trials claiming to be randomised controlled trials are often given greater weight than those from other research designs. It is doubly important, therefore, that researchers and readers of published papers be alert to the pitfalls that may compromise the validity of results from such research trials. It is always worth asking who is being randomised as well as what is being controlled for.

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- 1 Greenhalgh T. Assessing the methodological quality of published papers. *BMJ* 1997;315:305-8. (2 August.)

Did study require subjects to change sex?

EDITOR—In one of her articles on how to read a paper Greenhalgh quotes as an example of problematic description: "We approached 147 white American teenagers aged 12-18 (85 males) at a summer camp; 100 of them (31 males) agreed to participate."¹ She notes a recruitment bias towards females. This is an understatement: her figures indicate that the researchers were so biased towards females that seven unfortunate males were forced to change sex.

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- 1 Greenhalgh T. Assessing the methodological quality of published papers. *BMJ* 1997;315:305-8. (2 August.)

Home Office addicts index no longer exists

EDITOR—In their article on use of illicit drugs Gerada and Ashworth state that the chief medical officer maintains, at the Home Office, an index of addicts to help doctors in the clinical management of drug misusers and to provide epidemiological information on trends in drug misuse.¹ This index was closed on 1 May 1997. All doctors in England are now expected to continue to report treatment demands of drug misusers by returning reporting forms to their local drug misuse database, which provide anonymised data to the appropriate regional database. Information is not limited to opiate and cocaine misuse but includes any misused drug that generates demand for treatment.

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- 1 Gerada C, Ashworth M. ABC of mental health: addiction and dependence—I: illicit drugs. *BMJ* 1997;315:297-300. (2 August.)

Clostridium botulinum was named because of association with "sausage poisoning"

EDITOR—I wish to add some mustard to Aronson's recent diet of sausages¹ by suggesting that the bacterium *Clostridium botulinum* is indeed so called because of its pathological association with the delicatessen in question and not (as Aronson says) because of its shape. In 1793, 13 people in Wildbad, Germany, became ill after sharing a large sausage; six of them died.² Not long after this, Justinus Kerner, a district health officer in southern Germany, recognised the connection between sausage and a paralytic illness affecting 230 patients. He made "sausage poisoning," or botulism as it came to be known, a notifiable disease.³ It wasn't until 1897 that van Ermengen published the first description of the causative organism and showed the production of a toxin (later identified as type B) that induced weakness in animals.⁴ As far as I know, this account is accurate and free of boloney.

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