belongs to him; and he has seen so many prescribing fads come and go! So to assess compliance in asthma, as a general concept, does not seem so important after making sure that the patient's non-compliance is not related to another individually or socially solvable problem. We could also assess the principle of compliance in asthma. Compliance is a behaviour, the result of a complex association of attitudes and beliefs about the disease, drugs and medicine; it is closely related to the patient's personality. To improve compliance means to improve the patient's submission to the regimen when he might expect from his doctor, who acts on his behalf, a guidance on his autonomy, his freedom to choose between different possibilities, perhaps an intelligent non-compliance.

The patient needs help and understanding; he owns his body and destiny and, ultimately, is the best judge of his own interests, provided that he is properly informed, and remains the final master of the treatment decision and implementation. Compliance is a narrow path leading from efficacy to effectiveness; we have to make it easy and attractive to the patient-trekker who will choose it...may be.

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The assessment of therapeutic compliance by asthmatic patients

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The assessment of patient compliance with prescribed therapeutic regimens is notoriously difficult. The problems are greater when considering the treatment of asthmatic subjects due to the prominence of the inhaled route for the delivery of drugs. The methods employed fall broadly into two categories; those which are indirect, assessing only what drug may have been taken and, secondly, those which directly measure the presence of a drug, or associated marker substance, in a biological fluid. Neither are entirely satisfactory and ideally a combination of both should be employed.

The simplest indirect method is to ask the patient what drugs he has taken and how often. This can be on a simple retrospective basis or undertaken prospectively using diary record sheets. Although having the considerable advantages of being universally applicable and both simple and cheap, this method suffers from being the most inaccurate of any available. In general, patients are thought to over-estimate their actual drug use by between 30 and 50% [1]. Zora *et al.* [2] have reported that only one of seventeen diary sheets completed by asthmatic children was accurate to within 10 percent of the number of puffs used as calculated by inhaler weights.

Even when patients are aware that their statements will be verified by more objective measurements, they cannot be relied upon to give entirely truthful responses. Thus Zuckerman *et al.* [3] found cannabinoid metabolites in the urine of 35% of pregnant adolescents who had denied using cocaine, despite being informed that urine assays would be performed. Although this may not seem relevant to the use of more immediately legitimate drugs, it is in keeping with most other studies such as that reported by the author in which 11% of asthmatic patients who claimed to have inhaled salbutamol in the preceding four hours had no detectable drug in their urine. Patient questionnaires have generally been held only to result in deliberate over-reporting of drug use. However there is clear evidence that many patients deliberately report much smaller drug intakes than they have actually used - for example almost one in five patients seen in general practice had urine salbutamol concentrations much higher than predicted from their reported intake [4]. It has been suggested that patients who admit to poor compliance may be more amenable to compliance modifying strategies. Although to date there has been no prospective validation of this hypothesis it does further ensure that the patient questionnaire will remain as a central plank of compliance assessment strategies.

Regrettably the physician can give no more an accurate picture of his patient's compliance. Caron and co-workers [5] have shown that physicians of all levels of experience cannot predict which patients will follow their prescribed drug regimen. Use of records

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documenting collection of prescriptions will also over-estimate the true amount of drugs actually taken by the patient.

Since the patient cannot be relied upon to report his own drug consumption, attempts have been made to follow drug use by monitoring the amount of drug which remains unused. Counting returned tablets or weighing returned aerosol cannisters to determine the number of actuations offer the advantages of being suitable for prospective study and of monitoring compliance over a period rather than at a single time point. In addition these methods are devoid of false negative results (for poor compliance) as any tablets which remain in the bottle clearly cannot have been taken. The same cannot be said of a lack of false positive results and, when compared against other methods, tablet counts may over-estimate true patient compliance by nearly as great a margin. Weights of returned aerosols are particularly prone to over-estimate the actual amount of drug used due to the widespread practice of 'test firings'. The validity of this method is further impaired by the finding of STEWART [6] of return tablet counts suggesting perfect compliance in one third of patients who admitted to missing doses.

Automated counting devices such as bottles with microswitches in the lid have the advantage of allowing the pattern of drug taking to be monitored on a daily basis rather than yielding the bland overall mean compliance rates of total tablet counts. SPECTOR and co-workers [7] have studied the use of an automated device to record the actuation of a pressurised aerosol. Using the Nebuliser Chronolog they found only one third of patients were fully compliant with lodoxamide (a cromoglycate-like drug) for one month. The patients over-estimated their actual drug use by over 50%. However this approach still does not circumvent the fundamental problem of confirming that what came out of the bottle or aerosol necessarily went into the patient.

The final indirect method for the assessment of compliance is to monitor the therapeutic outcome. Although HORN, *et al.* [8] have clearly documented a correlation between compliance and reduction in the severity of asthma, failure of a therapeutic regime can only be ascribed to poor compliance if appropriate drugs are being prescribed in adequate dosage which historically has tended not to be the situation in the management of asthma.

All indirect methods to assess compliance fail to confirm actual ingestion of the drug by the patient. In contrast direct assay of either a drug or an associated marker in a biological fluid confirms that the patient actually took the drug. Although applicable to prospective studies drug or marker assays can only monitor compliance at relatively infrequent intervals and reflect only short-term drug use by the patient. They are also potentially subject to interference from intercurrent drug use or variations due to food or diurnal patterns of metabolism or excretion. In addition assay of drugs taken by the inhaled route is problematical because of the very small doses and the small proportion of drug which is actually retained within the body. Nonetheless using a method based on a high performance liquid chromatography (HPLC) assay of COLTHUP *et al.* [9], HORN *et al.* [2] have documented that salbutamol will be detectable in urine for at least four hours after inhalation of 200 μg of salbutamol. To date this is the only system suitable for large studies of compliance with inhaled therapy. Assay of drugs taken orally for the management of asthma is much easier and established assays are available for both prednisolone and theophylline. However, both drugs demonstrate marked inter-individual differences in pharmacokinetic handling and theophylline levels, in particular, are subject to interference from a multitude of confounding factors such as other drugs and the smoking status of the patient.

Attempts to circumvent the difficulties of monitoring compliance with inhaled drugs could potentially be made by the addition of trace quantities of either inert substances (*e.g.* riboflavine) or other agents (such as digoxin or phenobarbitone in pharmacologically inactive quantities). To date, despite extensive study of such methods and statements of the properties required [10] there have been no studies in asthmatic patients.

No single method of assessment of compliance with (anti-asthma) therapy is ideal nor does any one method give a full picture of the pattern of compliance. Usually the chosen method(s) will require to be validated specifically for the particular circumstances under investigation. Despite this, no study of a therapeutic regime can be considered fully valid without some documentation of whether the patients took their treatment.

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