COMMENT

I asked the chief tonometrist at the Princess Alexandra Eye Pavilion in Edinburgh to approve this form for recording intraocular pressure before I had it duplicated. She told me that it would not do. I wondered why—it was simple, neat, and unambiguous. Or was it? The patient's right eye is, of course, on the tonometrist's left as she faces the patient and ought to be so on the form also. Therefore the form should be redesigned as shown.

Time (hours)	Right eye	Left eye
09.00		
11.00		

If experience is the sum of one's errors then I, for one, have learned a vast amount, and one of the most valuable lessons is always to check out form design with the person who will do the recording and, for all but the simplest forms, to pilot them before the trial proper begins.[1] Useful pointers on form design have been given by Wright and Haybittle.[2]

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Clinical Topics

Compliance with drug treatment

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Compliance may be defined as "the extent to which the patients' behaviour coincides with medical or health advice."[1] The recommendation need not be for drugs, but may seek to modify the patient's lifestyle—for example, by a change in diet or smoking habits. We are concerned here only with the extent to which patients comply with prescriptions for drug treatment. Because it is difficult to define compliance, a precise assessment of the size of the problem is not possible. For practical purposes it might be reasonable to term a patient non-compliant when the failure to comply is sufficient to interfere appreciably with achieving the therapeutic goal. An alternative, which may be used for comparison, is to take an arbitrary level of compliance—for example, 80% of tablets consumed. Even then, the pattern of drug taking may be more important than the level of compliance. With antihypertensive treatment, for example, missing one complete week of treatment might result in high pressures with the attendant risk of stroke and heart failure, but the same number of doses missed over a three-month period would have no measurable effect on controlling blood pressure. The same reasoning could be applied to the use of anticonvulsant and oral hypoglycaemic agents. It is important therefore to see compliance in the context of the outcome of treatment, rather than to waste resources detecting levels of non-compliance that may not be clinically important.

Further confusion arises from failure to distinguish between the deliberate non-complier and the patient whose problem is one of failure to understand the prescribing instructions.[2] While the clinical outcome may be the same for both types of patient, the means of dealing with the problem will be very different.

Despite these difficulties in interpretation, the failure of patients to comply with prescriptions clearly represents an important problem. Estimates of the extent of non-compliance with short-term medication regimens have varied considerably, but the level of non-compliance may in some cases be as high as 92%.[3] Compliance with longer term medication appears to average about 50%.[2 4-7] Unfortunately, studies have often failed to establish a relationship between the level of compliance and the outcome of treatment, but, as the extent of the problem becomes more widely recognised, non-compliance is now often considered a possible reason when it is difficult to achieve the desired therapeutic response.

Determinants of compliance

The factors that we consider important in compliance may be considered in relation to the illness, the patient, the doctor, and the regimen. Often, it is the interaction between two or more of these influences that determines the adherence to the prescribed regimen. One cannot consider the demands of the regimen without examining the patients' ability to meet these demands. Similarly, the interaction between the doctor and patient may be of greater importance than the personality or attitudes of either considered in isolation.

THE ILLNESS

With the exception of patients with psychiatric illness, who are in general less compliant than patients with non-psychiatric

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diagnoses,[8] it has proved difficult to relate compliance patterns to particular diseases. Increasing severity of disease or symptoms is not necessarily related to improved compliance,[8 9] and, though increasing disability does appear to be associated with better compliance,[10] this may be due to the greater supervision given to the more disabled patients. In general, the longer the duration of treatment, the poorer is compliance likely to be.[3 8 9] Patients requiring long-term treatment—for example, those with hypertension or tuberculosis—are generally more likely to comply poorly.

THE PATIENT

Many studies[2 10–15] have sought a relation between compliance and socioeconomic factors, but in general no clearcut association has been found. Attention in particular has focused on the problems of the elderly. Since elderly people consume more medication than other age groups this attention may be justified, but, although the confused or elderly patient requires supervision, there is no convincing evidence that elderly people with good brain function are less likely than younger people to comply with a given regimen. Compliance appears to be similar among men and women,[9 10 12 13] and, while a higher educational standard might be expected to promote compliance, the many studies that found no association[9–11 13 14] between the two implies that other factors play a part. Economic status and social class may be important factors in compliance if eligibility for health care is limited.[15]

THE DOCTOR

The doctor is a most important influence on compliance because he directly determines so many other factors, not least being the actual regimen, and he is also in the best position to guide the course of the doctor-patient interaction, which is of great importance in determining the patient's response to recommended treatment. Features of this interaction that influence compliance are the extent to which the patient's expectations are met, his level of satisfaction with the visit, and the level of communication between the two.[11 13 16 17]

Another aspect of compliance less often considered is the concept of doctor compliance. Vidt[18] described this as the responsibility of the doctor to adhere to the optimum principles of management. When the prescription is inappropriate in some way, and should the patient experience unwanted effects, failure to comply must be seen as a protective response.[19] The observation that large quantities of unconsumed drugs are often found in patient's homes has rightly prompted speculation as to whether this represents non-compliance or misprescribing.[20]

REGIMEN

Manipulations of the regimen, such as reducing the number of drugs and the frequency of dosage and side effects, are commonly used to try to improve compliance. While excessively complex regimens with several different drugs undoubtedly have a negative effect on compliance,[2 6 8 11 21] there is little evidence that a once daily regimen is better than twice daily. A recent study with digoxin[22] showed that compliance as determined by tablet counting was considerably better with once or twice daily regimens than with a four times daily regimen, but there was no accompanying difference in steady-state plasma digoxin concentrations. There is also uncertainty as to the influence of side effects on compliance: some studies have shown that side effects cause non-compliance, whereas others have found no difference in side effects between compliers and non-compliers. When patients are asked the reasons for their non-compliance only 5-10% mention side effects.[6 15 17 21]

The effect of cost on compliance has not been fully investigated. Yet again, the evidence is conflicting, and providing drugs at low cost does not necessarily improve compliance.[23] Nevertheless, within some health care systems there are undoubtedly many patients for whom cost represents an important barrier to compliance.[6 8 15 24]

Measurement of compliance

Compliance may be measured directly by determining blood concentrations or urinary excretion of either the drug, a metabolite, or a marker. The technology needed to measure plasma or urine concentrations is considerable, but assay facilities for drugs such as digoxin and most anticonvulsant drugs are now widely available, and recent developments have provided simple and reliable methods of detecting many antihypertensive drugs.[25] Drugs with a long half life, the classical example being digoxin, give the steady state plasma concentration reflecting compliance over the previous week or more, and plasma concentrations of such drugs may provide useful information. For many drugs, however, it is not appropriate to measure plasma concentrations because a relatively short half life means that the plasma concentration indicates only whether or not the last dose has been taken.

Indirect methods of measurement are more generally applicable but lack precision. Failure to achieve an adequate therapeutic response is often the first clue that a patient is failing to take medicines. Since compliance is relevant only when it interferes with the therapeutic response, non-compliance detected in this way is important and deserves attention. Although it is not always reliable,[26] interviewing patients has the advantage that it may elicit the pattern of compliance and the reason for non-compliance. Also, patients who admit to non-compliance are more likely to respond to corrective measures.[27]

An estimate of compliance may be obtained at a clinic visit by counting the number of tablets remaining. The usefulness of this method depends on being able to determine how many tablets were originally dispensed. The more devious non-complier may adjust the number of tablets to appear compliant. Nevertheless, this method is more reliable than interview, and has the advantage of being easy to carry out. Special medication monitors providing a record of the removal of tablets from the container is also available, and their potential is being investigated.[28]

Strategies to improve compliance

Efforts to improve compliance must start with prevention, and here the doctor bears the main responsibility. He must be aware of the potential problem and encourage patients to comply, and must sustain this effort throughout the treatment. He must ensure that the patient understands not only the details of the regimen but also the need for treatment and the importance of any likely side effects. It may be useful to provide patients with written instructions about the regimen,[29] and information booklets about their condition can improve their understanding of the importance of treatment.[30] The regimen should be kept as simple as possible, avoiding excessive numbers of doses or preparations. It is rarely necessary to require patients to take drugs on more than two occasions a day, and inconvenient times should be avoided. Fixed ratio combination products are useful in reducing the complexity of the regimen.

Detection of the non-complier is the next step. Careful questioning at follow-up visits may detect non-compliance, particularly in those who have not responded to treatment. Tablet counts may be possible and in some instances the measurement of plasma or urine concentrations of drug may be justified.

Finally, an effort must be made to rectify the state of affairs when non-compliance is apparent. This may need only further

careful explanation of the regimen or the importance of treatment, or it may be necessary to adjust the regimen. Aids to compliance such as calendar packs or special dispensers may prove useful.[28 31] When compliance remains unsatisfactory, the help of a member of the patient's family may be sought, or it may be necessary ultimately to resort to a regimen which by its nature requires supervision—for example, parenteral administration.

In conclusion, the factors concerned in failure to comply with therapeutic regimens are complex. Rarely does a patient default for one single reason but rather because of a multiplicity of reasons that interact to produce a state of affairs in which compliance is difficult. The approach must be based above all on an awareness of the diverse nature of the problem and must seek primarily to prevent it. A high level of suspicion helps in detection, and various fairly common-sense ploys are readily to hand.

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Several of my patients whom I have encouraged to switch from butter to margarine on account of the benefit to the cardiovascular system have expressed alarm at the carcinogenic dangers mentioned recently in the press. What is your opinion on this?

While a change from butter to margarine would reduce cholesterol intake, a reduced intake of saturated fats is considered to be more effective in reducing blood cholesterol concentrations, and most authorities suggest that the dietary advice should be to reduce the intake of saturated fats and increase the intake of polyunsaturated fats—for example, by substituting for butter a margarine with a higher proportion of unsaturated fatty acids. It is generally agreed, however, that such a change should be accompanied by a reduced total fat intake.[1] The processes used in producing margarine may produce fatty acids that are normally present only in low concentrations in butter—in particular, fatty acids with a trans-configuration—but the suggestion reported in the press is at present a hypothesis that needs to be tested. The incidence of most cancers has been relatively static over the past century, and there is little evidence for any radical effects of food processing.[2]

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Is anything known about the aetiology of adenocarcinoma of the ovary? Is there any evidence of an increased incidence in relatives of patients with this condition?

The peak incidence of adenocarcinoma of the ovary is in the 60 to 70 age group, with the highest incidence in the professional classes. There is twice the chance of developing primary carcinoma of the ovary if the patient has had a carcinoma of the breast. Diagnostic radiography does not cause carcinoma of the ovary. It is thought that the incidence is increasing and that it was rare in the nineteenth century. There is an increased incidence in the unmarried and in infertile women. Ovulation is believed to be an aetiological factor, and there is evidence that long-term use of the pill possibly offers protection against this carcinoma. One theory is that ovulation produces a break in the capsule of the ovary through which potential carcinogens may enter. Substances introduced into the vagina can rapidly gain access to the peritoneal cavity through the uterus and tubes, and such substances as asbestos and talcum powder have been suggested as possible carcinogens. There is no evidence of a viral cause, and women who have had mumps have a lower incidence of carcinoma of the ovary. There does seem to be a radical variation, the highest incidence being in the Scandinavian countries and the lowest in the underdeveloped parts of the world, but Japan, though highly developed, has a low incidence. Japanese living in the United States, however, have the same incidence as American whites. In the Danish Twin Registry of 31 women who have had ovarian cancer, the twin was not affected. There are case reports of ovarian carcinoma running in families.

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