BLOOD LEVEL OR PHARMACOLOGICAL RESPONSE?

With the launching of a new journal devoted to Clinical Pharmacology, it is, perhaps, appropriate to consider what its terms of reference should be, and the breadth of its interests and responsibilities. Clinical pharmacology has been defined as the study of what drugs do to the human body and what the body does to drugs, both in health and disease (Prichard & Turner, 1971). This definition embraces two main approaches to the subject, namely the measurement of a subject's response to a drug in units which may be subjected to statistical analysis, which might be regarded as the pharmacodynamic aspect, and pharmacokinetic studies of its absorption, disposition and excretion. There is, at present, a danger that the development of sophisticated biochemical and pharmaceutical methodology, and the application of high-powered statistical computer-based techniques may lead to an inappropriate emphasis on the pharmacokinetic aspects (Turner, 1973). Dollery (1973) has recently drawn attention to this problem in an Editorial in the *European Journal of Clinical Pharmacology*, in which he comments on the increasing number of articles in journals of clinical pharmacology which are concerned with drug concentrations in plasma and other aspects of pharmacokinetics but which provide no data concerning the relationship between kinetic measurements and the pharmacological, therapeutic or toxic effects of the drug.

The therapeutic efficacy and safety of some groups of drugs, such as anticonvulsants, anti-dysrhythmics and lithium may certainly be improved by regular monitoring of plasma levels. Detailed studies of aminoglycoside kinetics have permitted the development of nomograms and digital computer programmes for calculation of dosage schedules for individual patients such as that for gentamicin by Dr Mawer and his colleagues on page 45 of this issue. It is hoped that the use of such aids to prescribing will give serum gentamicin concentrations within the chosen therapeutic range and reduce the risk of oto-

toxicity, particularly in patients with renal impairment.

In some cases, however, it is more convenient, and therapeutically more useful, to measure a patient's response to a drug rather than its blood level. The pharmacokinetic interactions between warfarin and other drugs, such as phenylbutazone or dichloralphenazone are complex, particularly if *in vitro* studies with concentrations bearing little, or no, relationship to *in vivo* levels are considered. While the results of such an interaction, therefore, are difficult to predict in any one patient, the result can readily be monitored by measuring his prothrombin time, and his treatment modified accordingly. Unfortunately, there are still only a limited number of instances in which a patient's response can be measured accurately and the measurement of the action of psychotropic, analgesic and anti-inflammatory drugs is very much more difficult. The development of methodology in these areas is slow, but as Dollery (1973) said, 'these problems can only be solved at the bedside and clinical pharmacology will not prosper if its practitioners spend too much time with the gas-chromatograph and too little with the patient.'

The use of kinetic models such as the nomograms described by Mawer and his colleagues have already proved of therapeutic value, but there is a danger that some others may be irrelevant or even misleading. After telling the old Russian story about a villager who wore spectacle frames without lenses and who, when asked why he did so answered 'It's much better than no glasses at all,' Lasagna (1972) made the point that bad scientific models can be worse than no models at all, because, like wrong lenses, they may distort all that is seen.

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