Clinical pharmacology methodology: introduction

In 1978, an editorial appeared in the British Journal of Clinical Pharmacology with precisely this title [1]. It introduced a series of review papers which were published over the next 4 years on methods of investigation in clinical pharmacology. This introductory editorial was remarkably prescient, in that it laid out some of the fundamental principles of clinical pharmacology and foresaw some of the ways in which it would develop. Professor Shanks emphasized the central role of investigation and measurement in diagnosis and assessment of patients, in understanding physiological processes in the investigation of adverse effects of drugs, and in helping to understand their mode of action. Not surprisingly, the series began with a dozen or so articles dedicated to the cardiovascular system. This was the time of an explosion in the discovery and development of such agents as the β -adrenoceptor antagonists and calcium channel blockers. The rapidly expanding methods of investigation in cardiovascular physiology and pathophysiology established fundamental principles in studying dose responses, defining specificity and selectivity of receptor subclasses and also paved the way for a better understanding of how older drugs such as the nitrates and diuretics might work. Shanks was also perspicacious in pointing out that 'the investigation of the effects of drugs is not, and should not be the exclusive province of the clinical pharmacologist (and cardiologist)'. This series was to set a high standard of investigation from which others could learn.

The cardiovascular system was followed by 'methods in' respiratory medicine, and in 1980 Lader & Richens [2] introduced a series on the central nervous system. This was followed in 1981 by an introduction to the kidney and urinary tract [3].

Measurements of responses in healthy normal volunteers and patients is fundamental to understanding drug action. Equally, the design of experiments, the analysis and presentation of results to the highest standards are essential so that decisions can be taken with confidence. Chaput de Saintonge & Vere [4] introduced a series on 'Problems In Clinical Trials' and pointed out the central role of the clinical trial in rationalizing the choice of treatments for patients, its place in minimizing bias and in replacing personal impression by objective evidence. These authors recognized, as many have done since, the difficulties of extrapolating from the controlled clinical trial to individual patients treated in a clinical setting. They stated, quite incontrovertibly that: 'a useful trial is one which has helped

to change the beliefs of doctors towards something which is more useful to patients than that which may have existed before it'.

Since those heady years, clinical pharmacology has expanded its boundaries quite remarkably to embrace molecular medicine, pharmacogenomics and pharmacoeconomics. Yet at the core, clinical pharmacology is still about measuring drug effects in man, be it in an individual, in a clinical trial or at a population level. Hence our new series in 'methods' will take some of these established principles and review what has changed in the intervening years. It will also look at the application of methods in the new disciplines. Unlike the previous articles, these reviews will not necessarily appear strictly by specialist area. Contributors at the forefront of their subjects are in increasing demand for articles and the Journal's first responsibility has to be to original papers. However, in the early part of the new millennium, we shall start publication of the series in five areas: cardiovascular and respiratory, statistics and clinical trial methods, molecular advances in cardiovascular medicine, and pharmacogenetics.

It is hoped that these series inform, educate and excite. They will also fulfil a practical and required function, i.e. contributing towards Continuing Medical Education. The Editorial Board would like to thank all those who have agreed to write or to commission these articles.

N. S. Baber

Medicines Control Agency, Market Towers, 1 Nine Elms Lane, London SW8 5NQ

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