CLINICAL PHARMACOLOGY METHODOLOGY: INTRODUCTION

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The development of scientific medicine during this last 30 years has extended to the study of the effects of drugs in man with the development of the speciality of Clinical Pharmacology.

While advances in the investigation of many different groups of drugs have occurred in recent years, cardiovascular clinical pharmacology, at least in the British Isles, has given the lead to the development and application of methods for the study of drugs in man.

Several factors have contributed to these developments. There has been the desire to increase our knowledge of the mode of action of drugs, which has been facilitated by the development of new methods for the investigation of cardiovascular function. Such methods have initially been applied to cardiac investigation and to cardiovascular physiology but their value in the study of the effects of drugs has then been appreciated. Increased realization of the importance of adverse effects has prompted the fuller investigation of cardiovascular effects of drugs to reduce the incidence or at least understand the mechanism of these effects. The continuous development of new drugs for the treatment of diseases of the cardiovascular system e.g. anti-dysrhythmic, hypotensive and positive inotropic agents, has provided a continuous and fruitful field for investigators, not only for documentation of their effects but also for their mode of action: such drugs must also be compared with their predecessors. The development of the scientific method has resulted in a greater demand for information about drugs based on sound factual evidence rather than on clinical impressions.

It has been decided by the Editorial Board of this Journal to provide a series of twelve to thirteen articles on Cardiovascular methodology in Clinical Pharmacology which will appear at monthly intervals. These papers will cover all main aspects of cardiovascular function. The cardiovascular system has been chosen as the first field because of the major advances and interests in this subject.

Interest in studying the effects of drugs in man continues to expand and many doctors who would not consider themselves clinical pharmacologists contribute to this subject. However it is important that new techniques are properly used, not only to ensure that the investigator gets the best return for the time and effort he has devoted to his observations but also that high standards of investigation are maintained.

One of the purposes of this series of articles is to provide an introduction to the essential basis of a wide variety of investigational procedures which are of value in studies of the effects of drugs on the cardiovascular system. Many investigators are familiar with some methods for cardiovascular studies but it is hoped that these articles will indicate other methods that might be of value.

In recent years sophisticated techniques have been developed for the investigation of the cardiovascular system primarily to help in diagnosis and assessment. Such techniques are of increasing value in the assessment of the effects of drugs and should be available for this purpose. However it is important that in such studies there should be applied high standards of practice of both pharmacology and cardiology. It is hoped that this series of articles will focus attention on the way in which these methods should be used in studies of the effects of drugs.

These articles are intended to show the range of methods that are now available for cardiovascular clinical pharmacology. The investigation of the effects of drugs is not and should not be the exclusive province of clinical pharmacologists or of cardiologists. There are many areas in which a considerable amount of new and essential information could be generated by others with lesser degrees of specialist knowledge by the use of equipment which is already available. The following are but two examples:

Arterial blood pressure is easily measured and the effects of drugs in patients with hypertension have been documented by physicians but often observations were casual and uncontrolled. The introduction of special sphygmomanometers to reduce observer error and bias were an advance. The more recent observations in which arterial pressure has been recorded continuously over a period of 24 h has indicated that some hypotensive agents may not be able to control arterial pressure throughout a 24 h period. The use of such techniques is of considerable importance in studying the effects of new hypotensive drugs and will be included.

Another example is the study of the effects of drugs on cardiac dysrhythmias. Until several years ago the electrocardiogram was observed or recorded for a short period before and after drug administration and a decision was made on whether the drug was or was not effective. Some drugs assessed in this way became widely used. The realization that dysrhythmias, especially after acute myocardial infarction, had an

inconsistent pattern indicated that such methods of assessment would be of little value in this connection. Consequently the development of systems for continuous recording of the ECG and especially of computer based systems for the analysis of such records for abnormal rhythms have been a considerable advance in the analysis of the effectiveness of anti-dysrhythmic drugs.

Striking advances have been made in other fields and it is hoped that many of these will be discussed in this series of articles.

Although the effects of some old but especially new drugs have been investigated in considerable depth, there are noticeable gaps in our knowledge about the effects of many drugs, not only of their pharmacological effect. It is hoped that this series of articles may stimulate some readers to investigate in more detail some of the drugs they are using.

I would like to thank everyone who has agreed to contribute to this series of articles, the first of which appears in this issue of the journal.