

The Oxford textbook of clinical pharmacology and drug therapy

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Preface

We have written this book with the needs of medical students in their clinical years paramount in our minds. Nevertheless, medical education is not restricted to the pre-qualification years, and we hope that the text may also prove of interest to those with more experience.

The book is composed of four sections. In Section I we have dealt with the general aspects of clinical pharmacology, our aim being to provide a scientific basis upon which a knowledge and understanding of drug therapy can be built.

Section II is brief and deals mainly with practical aspects of prescribing.

Section III is the drug therapy section, in which we have described the role of drugs in the treatment of disease. We have restricted ourselves to discussing drugs, and have not generally dealt with other matters concerned with the management of illness.

Section IV is a Pharmacopoeia. In this we have tried to bring together essential information about the majority of drugs mentioned elsewhere in the text. We felt that it was important to have this information in a separate section, but complementing the information about the use of drugs in disease. Too often the sciences of basic and clinical pharmacology are divorced from the practice of medicine, and one of our particular aims in writing this book has been to try to marry the scientific disciplines with the practical approach to drug therapy. The Pharmacopoeia will enable the student to recall those aspects of the basic and clinical pharmacology of individual drugs strictly relevant to the use of the drug in treatment, while the complementary drug therapy section will provide the means for understanding the role that each drug plays in the overall drug therapy of disease, interpreted in the light of the basic principles outlined in Section I.

We hope that this method of organization of the book, in addition to the information it contains, will enable the student to gain both the knowledge which is essential to the practice of safe and effective drug therapy and the understanding of how to effect that practice.

Some may be surprised that we have not included references. We did not feel this to be necessary. Instead we have included in Section II a chapter on sources of information, which for the interested student will lead to further reading.

We are conscious that in our approach to the subject we may not have hit on the ideal format first time round, and that there will be room for improvements. We shall welcome constructive criticism and suggestions.

There is a great deal of detailed information about drugs in this book, and we have tried very hard to make it accurate. However, it is always possible that errors have been missed, particularly in regard to the important matter of dosages. Furthermore, dosage schedules are constantly being revised and new adverse effects and drug interactions being described. For these reasons we urge all who use this book to consult pharmaceutical manufacturers' Data Sheets or other sources of information before prescribing or administering the drugs described in this book, or indeed any drugs. One cannot be too careful.

Oxford
June 1984

D. G. G.-S.
J. K. A.

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SECTION I

**Clinical pharmacology: the
scientific basis of drug therapy**

1 The four processes of drug therapy

The processes of drug therapy are very complex, although not more complex than those processes which underlie the illness for which therapy is being given. Historically modern drug therapy has developed from the herbal and folklore medicine of the past with its mixture of magic, empirical pharmacology, and faith of the patient in the doctor. Some cynics might hold that not much has changed! However there *have* been changes, even though the magic of drug therapy is still a potent force in its success. The changes which have occurred are in the understanding of the modes of action of the drugs we use and in the optimal application of those drugs to the treatment of disease. Underlying all this is an immense amount of work in the sciences of basic and clinical pharmacology.

The rationalization of drug therapy has lagged behind the understanding of disease processes for obvious reasons. The rational man obviously wants to be able to understand a pathological process and to make a precise diagnosis before instituting treatment. Until quite recently few specific and effective therapies were available and it is not, therefore, surprising that medical education and training has concentrated upon the art and science of diagnosis and the minute understanding of disease processes, neglecting, to a great extent, their treatment with drugs. The art and science of surgical treatment was not so neglected because manifestly *it* is profoundly effective in appropriate cases and demonstrates in a most dramatic way the doctor's concern and masterly activity on behalf of his patients.

In recent years, however, drug therapy has been undergoing a process of increasing rationalization. Advances in the understanding of the detailed events underlying the pathology of disease have allowed their manipulation with drugs. Conversely the empirical development of drugs useful in specific diseases has led to improvements in our understanding of those diseases. For example, the discovery of the precise biochemical abnormality in Parkinson's disease has led to the introduction of specific therapy with levodopa, while the study of the mode of action of psychotropic drugs has been one of the major factors in promoting the biochemical and pharmacological investigation of brain function in relation to mental disease.

4 *The four processes of drug therapy*

One of the main aims of the approach to therapeutics outlined here is to analyse drug therapy within a discipline as strict as that by which a diagnosis is reached. It does not matter that in the course of this analysis there may arise questions to which there are at present no answers, for only by asking such questions can we begin to understand the depths of our understanding or ignorance.

The approach which we shall describe is one in which drug therapy is analysed step by step by various processes. The scheme as outlined can be applied to any type of drug therapy and, more attractively, can be applied to optimize any individual patient's drug therapy.

There are four main processes involved in drug therapy (see Fig. 1.1). They are:

1. The pharmaceutical process.
2. The pharmacokinetic process.
3. The pharmacodynamic process.
4. The therapeutic process.

These four processes can be more simply formulated as simple questions, one for each process:

1. Is the drug getting into the patient?
2. Is the drug getting to its site of action?
3. Is the drug producing the required pharmacological effect?
4. Is the pharmacological effect being translated into a therapeutic effect?

1.1. PHARMACEUTICAL PROCESS: Is the drug getting into the patient?

The pharmaceutical process is concerned with all those factors inherent in the pharmaceutical formulation and presentation of a drug preparation which determine whether or not it is absorbed (in the case of oral, rectal, or parenteral administration) or reaches the appropriate site of action for an appropriate time in the desired form (for topical preparations). Strictly speaking we are not here concerned with the process of absorption itself but with the properties of the drug preparation, e.g. tablet content of drug, drug crystal size, tablet compression, excipients, and predictability of tablet properties such as rates of disintegration and dissolution.

Although it is not strictly relevant to the pharmaceutical process it is convenient here to remember to consider the question of patient compliance since that is an important factor in determining whether or not the drug gets into the patient.

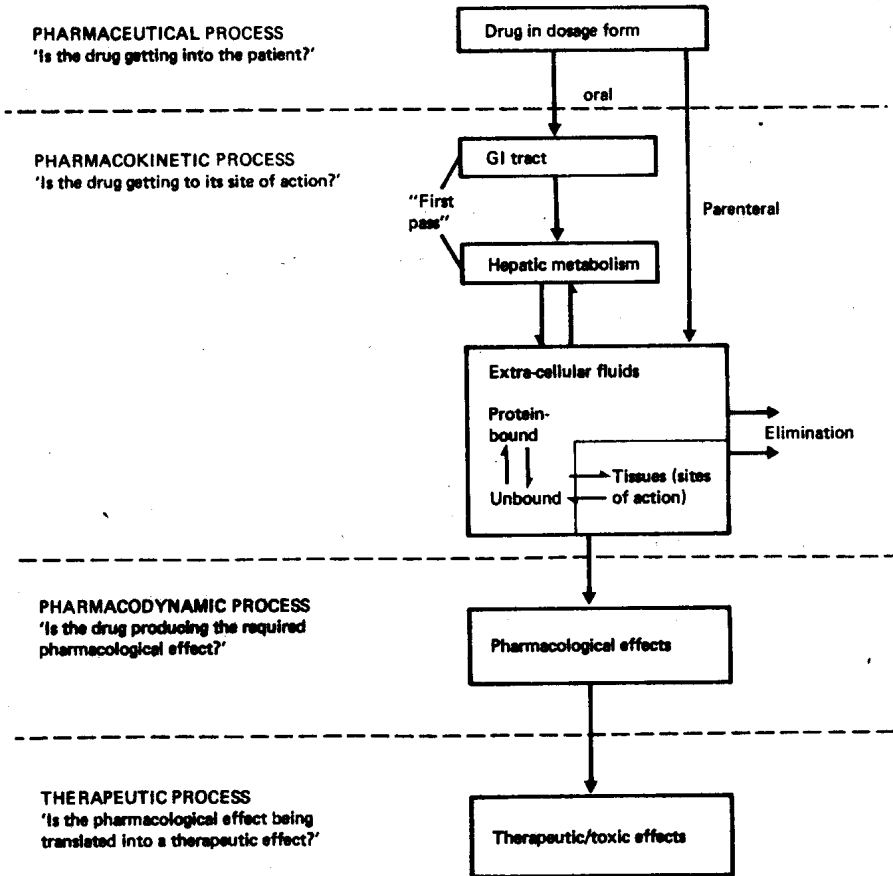


Fig. 1.1. The four main processes involved in drug therapy. Compare this figure with Fig. 6.1 in which more detail is given.

1.2. PHARMACOKINETIC PROCESS: Is the drug getting to its site of action?

The pharmacokinetic process is concerned with the absorption, distribution, and elimination (by metabolism and excretion) of drugs. It can be studied in the patient by measurement of drug and metabolite concentrations in blood and/or urine over periods of time after dosing. It is evident that, however many structural and metabolic barriers drug molecules have to pass, the concentration of a drug at its site of action must have the blood concentration as one of its major determinants. Thus, proper mathematical description of the pharmacokinetic characteristics of a drug can provide a great deal of information of relevance to both the pharmacological and the therapeutic or toxic effect.