Sixth Edition

Drugs in Anaesthetic Practice

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Butterworths

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Preface to the first edition

The modern practice of anaesthesia necessitates a considerable knowledge of physiology and pharmacology. Not only should the anaesthetist know about the action and side-effects of those drugs that he uses himself, but also about those employed by his surgical and medical colleagues on the patients he is called upon to anaesthetize, as they may have a marked influence on the course of anaesthesia.

We have therefore included not only those drugs which produce anaesthesia and analgesia and those controlling their complications, but also others which may have some influence on their course. Some drugs have been included because of their historic interest or because they have become the yardstick by which other drugs are measured; even though they are not now used in clinical practice they may still be of experimental interest.

We hope that the book will be of assistance to students studying for higher examinations in anaesthesia and to practising anaesthetists who require a book of reference. We think surgical students will also find it useful as their ever increasing curriculum requires a knowledge of many of the drugs and problems discussed.

The classification of the drugs described has caused some difficulty. As far as possible they have been grouped according to their main actions and the purposes for which they are used. There have had to be some exceptions, as if a drug could be placed in one of several groups an arbitrary decision had to be made. Much of the information given is well known and references are not needed; where, however, recent research has brought new facts to light, or when well summarized accounts of certain problems have been quoted, appropriate references are included.

Each section is preceded by a general article on the drugs concerned, and this is followed by monographs on individual drugs. Other articles have been included to link up various sections, especially where the drugs concerned are described in other groups. It is suggested that whenever a monograph on an individual drug is consulted it should be read, if possible, in conjunction with the general article on the group. In the text, *BP, BPC*, or approved names of drugs are used throughout; chemical names, synonyms and trade names are given under the headings of individual drugs.

Although new drugs are continually being produced by pharmaceutical firms, few prove of sufficient value to pass the test of time. Older drugs, thought to be of therapeutic benefit on empirical grounds, may eventually prove to be ineffective, some even harmful. We have tried to keep up to date, and much of the script written earlier has been revised recently. We are, however, conscious of the fact that in the course of time reconsideration of the value of certain drugs, especially the newer ones, will be necessary.

We would like to extend our special thanks to Dr C. L. Cope for writing for us the section on Corticosteroids, and to Dr P. J. Horsey for that on Electrolytes and Infusion Fluids. Our thanks are also due to Dr J. B. E. Baker for his advice and assistance during the early stages of the book, and to Mr C. R. Day of May and Baker Ltd, whose help with the preparation of drafts, advice on pharmaceutical aspects of drugs and the production of facts and figures has been of great value.

It is with considerable pleasure that we also acknowledge the helpful criticism and advice of our many colleagues whom we have consulted, and the patience of Butterworths, our publishers, during the time that the book has been in preparation.

Finally, we want to thank Joan Wood-Smith for much secretarial help and for looking after us so patiently during our many meetings.

Geoffrey Wood-Smith
H. C. Stewart

Preface to the sixth edition

With this edition we welcome Professor Harold Schnieden as co-author and wish Professor Stewart a happy retirement. Professor Stewart has been associated with this book since its inception and a tower of strength in the preparation of earlier editions. We look forward to an equally fruitful association with Professor Schnieden. Harold Schnieden is an examiner in the Primary FFARCS and thus well acquainted with the needs of trainee anaesthetists. He has also undertaken much research in areas of pharmacological interest to anaesthetists.

We have been fortunate in being able to retain the help and advice of our existing collaborators, Professor C. M. Conway (chapter 4), Professor D. Williams (chapter 19), Dr R. Fletcher (chapter 18) and Dr P. Horsey (chapter 20), who have revised their respective contributions.

As usual, we have needed to introduce monographs or short notes on drugs introduced since the previous edition and have cut out a few which have now been removed from general circulation.

In this edition greater use has been made of illustrations, particularly in chapter 1 on General Pharmacology, and we are indebted to Dr Carpenter (University of Manchester) for drawing these. In an effort to prevent the book becoming unnecessarily large, we have introduced 'small print' sections, not as traditionally thought of for the arcane, exotic, or unimportant, but for drugs that closely resemble others on which full monographs are included, in an endeavour to pick up any minor differences. We have also reduced the number of references; enquiry reveals that our readers very rarely consult them. We hope, on balance, therefore, to provide better value for money with this edition.

With this edition we also bid farewell to Mr Day, who has undertaken the indexing, preparing the converters, and checking the pharmaceutical information since the inception of the book. We welcome Dr Rees, also of the University of Manchester, who has compiled the Appendix on drug name converters.

One particular problem that creates increasing difficulty in preparing new editions is the growing practice of pharmaceutical companies to promote (and journals to publish) studies on drugs ahead of general marketing. It is not uncommon for such studies to figure widely in the literature for several years before the drug is obtainable for routine use. Such drugs may be available in the UK long before being available in the USA or vice versa, due to differing attitudes of the relevant regulatory bodies. Examiners appear to expect candidates to be knowledgeable about these drugs, and there is often no hard information as to when the drug will be available and indeed no guarantee that it ever will be. Our approach has been to include a monograph when we are reasonably confident that

the drug will be available during the life of the edition and to include a synopsis on what is currently known about such a drug at the time of preparation of the manuscript when the future is uncertain. It is an unfortunate fact of publishing life that the completion of the manuscript precedes publication by up to a year and we apologize in advance for any bad guesses in this respect.

Despite the numerous changes, the aims of the book remain unchanged, namely to provide a general textbook of pharmacology of special relevance to the practising anaesthetist, written particularly with the trainee in mind, and a reference source for the drugs that anaesthetists employ themselves or which are commonly given to their patients.

Professor Vickers gratefully acknowledges the assistance of Sara Marshall in undertaking numerous tasks associated with the preparation of the manuscript for the printers. Professor Schnieden is indebted to his secretary, Mrs V. Sillivan, for her word processing skills and her meticulous checking of the data presented to her.

M. D. Vickers
Geoffrey Wood-Smith

Contents

1

General pharmacology

The *Concise Oxford Dictionary* defines a drug as 'a medicinal substance'. Implicit in this definition is that a drug should be used for a therapeutic purpose. There are other definitions of a drug: for example, it has been defined as 'any chemical agent which affects living processes'. This is an all-embracing definition, for included in it would be environmental pollutants and food additives. To talk of 'the pharmacological action of a drug' is somewhat misleading as drugs do not really have actions: it is the tissues which have responses. Drugs commonly act by increasing or decreasing the normal physiological actions of a functioning tissue.

Mechanism of action of drugs

There are numerous ways in which drugs can produce their therapeutic effects. They can act on specific sites (receptors), initiating or impeding the normal response. They can raise or lower the concentration of a transmitter or modulator; for instance, a drug that inhibits the enzyme responsible for metabolizing a particular transmitter can effectively prolong its action. Some drugs by virtue of their physical properties act non-specifically. General anaesthetics are thought to act in this way.

Drugs usually have a single type of action on a tissue. In the intact organism, however, the direct response of a tissue to a drug may be modified by indirect actions due to drug effects on other tissues. Thus noradrenaline would increase cardiac rate by a direct action on the heart. However, if given intravenously to man heart rate falls due to a reflex bradycardia produced by the rise in mean arterial blood pressure – noradrenaline, by increasing peripheral resistance, causes the rise in blood pressure. Many drugs, especially those acting on the CNS, may have biphasic actions, initial stimulation being followed by depression.

Although many drugs are highly selective in their action, some are unfortunately not so selective, and their side effects may seriously upset the patient to the point of totally precluding their use. Toxic effects such as liver damage or agranulocytosis are even more serious, and patients taking drugs known to be likely to cause these complications must be carefully watched.

The response to a drug often varies in different individuals. The expected effect may not occur, there may be an abnormal response, or the drug may be without effect. These variations in effect may be due to the size of the dose, the route by which it is administered, the condition of the patient at the time, the presence of other drugs in the body, or sensitivity or resistance of the patient's tissues to the drug.

Although drugs with similar chemical structures often have similar actions, minor changes in structure may totally change the activity of a drug. Sometimes an