

TEXTBOOK OF
DENTAL PHARMACOLOGY
AND THERAPEUTICS



一九九二年九月七日

TEXTBOOK OF DENTAL PHARMACOLOGY AND THERAPEUTICS

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Oxford New York Tokyo
OXFORD UNIVERSITY PRESS

1989

1989

Oxford University Press, Walton Street, Oxford OX2 6DP

Oxford New York Toronto
Delhi Bombay Calcutta Madras Karachi
Petaling Jaya Singapore Hong Kong Tokyo
Nairobi Dar es Salaam Cape Town
Melbourne Auckland
and associated companies in
Berlin Ibadan

Oxford is a trade mark of Oxford University Press

Published in the United States
by Oxford University Press, New York

© John G. Walton, John W. Thompson, and Robin A. Seymour, 1989

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British Library Cataloguing in Publication Data

Walton, J.G.
Textbook of dental pharmacology and
therapeutics
I. Dentistry

I. Title. II. Thompson, John W.
III. Seymour, Robin A.
617.6

ISBN 0-19-261823-7
ISBN 0-19-261235-2 (Pbk)

Library of Congress Cataloging in Publication Data

Walton, J. G.
Textbook of dental pharmacology and therapeutics/J.G. Walton,
John W. Thompson, and Robin A. Seymour.
(Oxford medical publications)
Includes bibliographies and index.

1. Pharmacology. 2. Dentistry. I. Thompson, John W. (John Warburton)
II. Seymour, R. A. III. Title. IV. Series.

[DNLM: 1. Dentistry. 2. Pharmacology. QV 50 W239t]
RM300.W36 1989 615'.1—dc19 88-28909 CIP

ISBN 0-19-261823-7
ISBN 0-19-261235-2 (pbk.)

Typeset by Cotswold Typesetting Ltd, Gloucester
Printed in Great Britain
at the University Printing House, Oxford
by David Stanford
Printer to the University

THIS BOOK IS DEDICATED TO:

The memory of my Father and Mother (J.G.W.);

Judith, Jonathan, and Georgina (J.W.T.);

Gayle, Tom, and Oliver (R.A.S.)



FOREWORD

ROY STORER

Dean of Dentistry, University of Newcastle upon Tyne

THOSE conversant with the publications on Dental Pharmacology will recall the highly successful British Dental Journal booklet entitled *Pharmacology for the Dental Practitioner* by Mr John Walton and Professor John Thompson. They have been joined by Dr Robin Seymour in this textbook which is an expansion of that earlier publication. John Walton has been lecturing to dental students on pharmacology since 1960 and John Thompson began his academic career in medical pharmacology by presenting a course to dental students. Robin Seymour is a more recent addition to the Newcastle team and he has developed a particular interest in analgesics. The three authors have encouraged others in the Sub-Faculty of Dentistry at Newcastle to participate in research in the pharmacological field and the projects will be a valuable contribution to pharmacology in relation to dentistry, which is emerging as a specialist subject within the dental curriculum.

In this book, the authors have not only dealt with, in appropriate detail, those drugs used by the dentist but also those the dentist is likely to encounter in patients who are receiving medication from their medical practitioners.

As an increasing proportion of the population move into the elderly category, it is likely that more of those who seek dental health care will be on long-term medication. Therefore it is very important that the dental practitioner should have 'a thorough understanding of the principles of pharmacology so that he can anticipate drug interactions, allergies, incompatibilities, side effects, and other dangers.' (An Inquiry into Dental Education—A Report to the Nuffield Foundation, 1980, The Nuffield Foundation, London).

The chapter on Emergencies in Dental Practice is based on the authors' annual postgraduate course for dental practitioners in the Northern Region, which must be one of the most successful of its kind.

This book will be appreciated by undergraduates, by those studying for higher diplomas, and, not least, by general dental practitioners who, in the provision of whole mouth care for their patients, will be better able to deal with those who are on complex medication.

March 1988



PREFACE

OVER the past 30 years or so the subject of pharmacology has developed explosively with the result that there are now many groups of potent drugs used for the treatment of disease. This has had two important consequences for dentistry. First, a number of the newer drugs have found important roles in dental treatment. Second, many patients who attend for dental treatment are taking drugs for the treatment of medical conditions and it is therefore important for the dentist to be aware of this fact and to be fully conversant with the pharmacology and rationale behind the use of these drugs. Furthermore, it is obviously important for the dentist to be aware of the unwanted effects that may be produced by the drugs prescribed, some directly concerned with the mouth. Of equal importance is the need to know about possible interactions that might occur (and must therefore be avoided) in the event that the dental practitioner prescribes one or more drugs for dental treatment that have the potential to interact with those already being taken by the patient for medical reasons. Thus the need for the present-day dental student and dental practitioner to have a sound working knowledge of pharmacology and therapeutics is a pressing one, and this book has been written to meet these needs.

The book is divided into two sections. The first deals with general pharmacological principles together with those drugs that are part of the day-to-day pharmacological armamentarium of the dental practitioner. The second part deals with the pharmacology and therapeutics related to drugs which, although unlikely to be prescribed by the dental practitioner, are nevertheless of considerable importance for reasons already given.

This book is based on an earlier and much shorter book entitled *Pharmacology for the Dental Practitioner*, which was written by two of the authors of the present book (J.G.W. and J.W.T.). That original book has now been expanded into a comprehensive textbook for dental students and dental practitioners and, in tackling this difficult and lengthy task, the original authors have had the good fortune to acquire the invaluable help of Dr Robin Seymour, who has for some time assisted his colleagues in the teaching of pharmacology to dental students.

The authors are grateful to many colleagues and others who have willingly helped in various ways, and the names of these individuals are listed in the Acknowledgements. However, the authors alone are responsible for any errors of omission or commission that are to be found in this book. Furthermore, they would be most grateful to any reader who takes the trouble to point out mistakes or to make suggestions for a further edition.

Newcastle upon Tyne
February 1988

J.G.W.
J.W.T.
R.A.S.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the generous help and assistance they have had from colleagues in the preparation of this book. Those who have kindly read, and constructively criticized various chapters or sections of the text include Dr Heather Ashton, Professor R. W. F. Campbell, Dr T. S. J. Elliott, Professor B. T. Golding, Professor C. J. Hull, Professor M. D. Rawlins, Dr P. A. Routledge, and Mr A. K. Watson (Astra Laboratories). They also wish to acknowledge the valuable help given by the Audio Visual Centre and the Medical and Dental Library of the University of Newcastle upon Tyne. They are deeply indebted to Mrs Margaret Cheek for her tireless work in typing the seemingly endless drafts and also for her conscientious and painstaking labours concerned with the bibliography of this book. The help and forbearance of the staff of Oxford University Press is gratefully acknowledged. Finally, the authors wish to thank Mrs Judith Thompson for her help in preparing the index.

FIGURE AND TABLE ACKNOWLEDGEMENTS

The authors of this book wish to thank the following authors, editors, and publishers for kindly granting permission to reproduce published material as indicated.

Fig. 1.1: Adapted from Fig. 1.1 on p. 5, Grahame-Smith, D. G. and Aronson, J. K. (1984). *Oxford Textbook of Clinical Pharmacology and Drug Therapy*. Oxford University Press, Oxford. Fig. 1.4: Redrawn from Fig. 1, p. 201, Brodie, B. B. (1964). *Absorption and Distribution of Drugs*, (ed. T. B. Binns). Livingstone, Edinburgh. Figs. 1.5 and 1.6: Based partly on Fig. 2, p. 37, Gillette, J. R. (1967). In: *Drug Responses in Man*, (eds. G. Wolstenholme and R. Porter). Churchill, London. Based partly on Fig. 1, p. 17, Brodie, B. B. (1964). *Absorption and Distribution of Drugs*, (ed. T. B. Binns). Livingstone, Edinburgh. Fig. 1.7(b): Fig. 1, p. 995, Drew, G. C., Colquhoun, W. P., and Long, H. A. (1958). Effects of small doses of alcohol on skill resembling driving. *British Medical Journal*, 2, 993-9. Fig. 1.9: Fig. 2.2, p. 22, Creasey, W. A. (1979). *Drug Disposition in Humans*. Oxford University Press, Oxford. Fig. 1.10(a and b): Fig. 13.8, p. 189, Rowland, M. and Tozer, T. N. (1980). *Clinical Pharmacokinetics: Concepts and Applications*. Lea and Febiger, Philadelphia. Fig. 1.12: Fig. 3-10, p. 27, Schild, H. O. (1980). *Applied Pharmacology*. Churchill Livingstone, Edinburgh. Tables 1.3 and 1.4: Adapted from Table I, p. 453, Lefkowitz, R. J. (1979). Direct binding studies of adrenergic receptors: biochemical, physiologic and clinical implications. *Annals of Internal Medicine*, 91, 450-8. Table II, pp. 68 and 88, Lefkowitz, R. J. and Hofman, R. J. (1981). New directions in adrenergic receptor research. Parts I and II. In: *Towards Understanding Receptors*, (ed. J. W. Lamble). Elsevier/North Holland, Amsterdam. Table 1.5: Adapted from Fig. 1, p. 228, Koch-Weser, J. (1972). Serum drug concentrations as therapeutic guides. *New England Journal of Medicine*, 287, 227-31. Fig. 6.1: Thompson, J. W. (1984). Pain: mechanisms and principles of management. In: *Advanced Geriatric Medicine 4* (ed. J. Grimley Evans). Pitman, London. Fig. 13.1: Adapted from Fig. 8-16, p. 25, Schmidt, R. F. (ed.) (1978). *Neurophysiology*. Springer-Verlag, New York, Heidelberg, Berlin. Fig. 13.3: Wilson, A. and Schild, H. O. (1968) *Applied*

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General principles of drug action

THE word 'pharmacology' means nothing more nor less than the study of the effects of chemical substances upon living tissues; it is derived from two Greek words; *pharmakon*, drug; *logos*, study. Living cells, tissues, and organs consist of biological systems and a chemical substance that is capable of modifying a biological system in a relatively selective way is known as a drug. Whilst many chemical substances could be said to fall into this category, only a small proportion of them are sufficiently selective and safe to use for the prevention or treatment of disease or, in other words, as therapeutic agents. For example, phenol and many other chemical substances when applied to nerves can block impulse transmission but cannot be used for this purpose routinely because they cause irreversible damage to nerve tissue. The actual number of clinically acceptable local anaesthetics used by the average dental practitioner can be counted on the fingers of one hand.

The rapid increase in the number of new drugs during the past quarter century has been aptly described as the 'drug explosion'. Prior to this, the number of drugs of real value was very small; there were many virtually useless preparations but they did not do much harm even if they did not do much good! Today, the situation is vastly different; a bewildering and ever-increasing number of new and powerful drugs is available for therapeutic use. The subject of pharmacology has developed at a phenomenal pace, particularly when one considers that it was only in the 1930s that it crystallized out as a separate subject from related disciplines such as physiology and chemistry (Paton 1963). Pharmacology has received its greatest impetus from progress made in the field of synthetic organic chemistry and the momentum has been maintained by the ever-present need for chemical substances that can be used to prevent or control disease.

The dental practitioner, in the same way as the medical practitioner, is faced with the problem of keeping abreast of developments in pharmacology and therapeutics. In order to use drugs rationally, it is important to understand the basic principles of drug action. The clarification of old ideas of drug action coupled with the discovery of new mechanisms have made it possible to begin to interpret the effects of drugs in terms of molecular events governed by physico-chemical laws. The stage has therefore been reached when it is now possible to enumerate the different processes involved in the absorption, distribution, mechanism of

action, fate, and excretion of drugs. Furthermore, it is in the study of the mechanism of drug action that major progress has been achieved. Sufficient knowledge is now available to make it possible, in many instances, to present a coherent account of the action of a drug. It is the authors' fervent belief that the administration of any drug, irrespective of type and route, should always be carried out with these principles constantly in mind. Drugs will come and drugs will go; but basic principles will always remain even though these may be modified and extended as new knowledge becomes available.

The dental practitioner most commonly applies drugs locally; much less often is he or she concerned with their systemic administration, with the exception of analgesics, antibiotics, and drugs used for sedation. Nevertheless, many of the same pharmacological principles apply whether the drugs are used systemically or locally. When a drug is given locally, some proportion of the total dose will be absorbed into the general circulation, the amount depending upon the drug, the dose, and the area to which it is applied. It is possible therefore that under certain conditions, local application of a drug may be followed by undesirable systemic effects. Today, many patients who come to the dental surgery are already taking drugs prescribed by their medical practitioners or even by themselves. The dental surgeon should always be aware of the risk of a drug interaction between the drug(s) to be prescribed and those the patient is already taking. Thus, the problem of drug interaction is another reason why the dental practitioner needs to be conversant with the general principles of drug action. This is also an appropriate moment to remind ourselves of a particularly important point, namely, that to the layman the word 'drug' usually means something different from that understood by the prescriber. Furthermore, in the mind of the average patient, there is often a vast difference between the meanings of the words 'drug', 'pill', 'tablet', 'medicine', and 'mixture'. If this is not appreciated by the practitioner the fact that a particular patient is under the influence of a powerful drug may be missed to their possible detriment.

SOURCE OF DRUGS

In the past, drugs were obtained from natural sources and some of the most important drugs are still derived in this way. For example, insulin is obtained from the pancreas of cattle or pigs; digitalis from certain species of the foxglove plant; and iron, commonly used in the form of ferrous sulphate, is derived from mineral sources. Nevertheless, today, the majority of drugs are synthesized by chemists and every year many thousands of new compounds are made and screened for possible use as drugs. Table 1.1 indicates the stages involved in the development of a drug (Thompson 1967; Goldberg and Griffin 1984; M. D. Rawlins, personal communication). It also shows the points at which the Committee on Safety of Medicines operate in order to weigh the evidence about new drugs submitted to it by the pharmaceutical industry and by the dental and medical professions, so that

Table 1.1. Development of a drug

Principal individual(s) concerned	Stages in the development of a drug	Regulatory involvement
Various	Ideas	
Chemist	Natural or synthetic chemical compounds	
Pharmacologist Biochemist	Pharmacological tests including: pharmacodynamics } in animals pharmacokinetics }	
Toxicologist	Acute toxicity (e.g. LD ₅₀) Chronic toxicity tests including studies on two species of animals, one rodent and the other non-rodent Reproduction toxicity (fertility and reproduction teratogenesis, fetal and embryological toxicology) Mutagenicity Carcinogenicity	
Pharmacist	Pharmaceutical formulation Clinical trials	
Clinical pharmacologist Normal volunteers	Phase 1: a pilot investigation made in a small number of normal volunteers	
Dentist/Doctor Clinical pharmacologist Nurse Patients Statistician	Phase 2: an 'open' clinical trial carried out in a small number of patients Phase 3: large-scale clinical trial (double blind)	Clinical trial certificate (or clinical trial exemption) required
Practising dentists/doctors and their patients	Phase 4: monitored release and post-marketing surveillance of new drug Accepted drug	Product licence required Post-marketing surveillance For unforeseen reasons, usually toxicological, it may prove necessary to withdraw a drug at a time

it can act as an independent assessor. As can be seen from Table 1.1, the development of a drug is a long and complicated process involving many stages and many individuals.

CLASSIFICATION OF DRUGS

The most logical way to classify drugs would be according to their mechanism of action, but this is not yet feasible because for many drugs this information is still

incomplete. One of the largest areas where knowledge is lacking concerns drugs which act on the central nervous system, a situation which is slowly improving as new knowledge becomes available about the biochemistry and pharmacology of the brain.

At present, the most practical way to classify drugs is according to their main site(s) of action and this is the method adopted by (see Chapter 3) the *British National Formulary* and also by the *Dental Practitioner's Formulary* (a joint publication of the British Dental Association, the British Medical Association, and The Pharmaceutical Society of Great Britain).

MODE OF ACTION OF DRUGS

The subject of pharmacology exists because a large number of substances exert a selective action, so modifying the behaviour of some cells or tissues more than others. Indeed, were it not for selective action, it would be impossible to use chemical substances therapeutically. Unfortunately, with many of the drugs at present available, the degree of selective action is less than is desirable, so that in order to produce the required effect it may be necessary to use a dose that also gives rise to certain unwanted actions. In some instances these are of trivial inconvenience to the patient but in others, unwanted effects of a more serious nature may occur. Pharmacologists, particularly those in the pharmaceutical industry, are constantly striving to produce drugs that exert a higher degree of selective action than existing drugs of the same type. However, it is likely to be a long time before the majority of drugs available exert such a high degree of selective action that they are incapable of producing any unwanted effects.

THE PROCESSES OF DRUG THERAPY

Four main processes are involved in drug therapy:

- (1) the pharmaceutical process;
- (2) the pharmacokinetic process;
- (3) the pharmacodynamic process;
- (4) the therapeutic process.

As has been pointed out by Grahame-Smith and Aronson (1984), each of these four processes can be formulated as a simple question:

- (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?

These closely interrelated processes will now be discussed in detail and Fig. 1.1 illustrates them diagrammatically.