# AN INTRODUCTION TO PHARMACOLOGY AND THERAPEUTICS

BY

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NINTH EDITION

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# BRITISH PHARMACOPOEIA 1958

## ADDITIONS AND DELETIONS

The *British Pharmacopoeia 1958* will be published in March and will become official in September 1958. Consequently a number of drugs mentioned in the text as official, will cease to be so, whilst others not so mentioned will acquire official status. All such changes which affect any drug mentioned in the text of this book will be found in the lists given in these endpapers or in those at the back of the book.

The publishers wish to express their gratitude to the General Medical Council for supplying the information from which these lists have been compiled and for their permission to publish it.

### ADDITIONS

DRUGS MENTIONED IN THE TEXT. For ease of reference the page on which the principal entry occurs in the text is given in the adjacent column.

DRUGS NOT MENTIONED IN THE TEXT. It is not intended to give a complete list of additions to the B.P. 1958 of drugs not mentioned in this book, but the following are included, although in the interests of space they were omitted from the text.

*Acetazolamide*

*Amylobarbitone*

*Atropine Methonitrate*

*Chloraquine Sulphate Injection*

*Diphtheria and Pertussis Vaccine*

*Diphtheria, Tetanus, and Pertussis Vaccine*

*Human Gamma Globulin*

*Hyaluronidase*

*Mustine Hydrochloride*

*Oxytetracycline and Procaine Injection*

*Paramethadione*

*Procainamide Hydrochloride*

*Procyclidine Hydrochloride*

*Propyliodone*

*Sodium Chloride and Dextrose Injection*

*Sodium Radiophosphate ($^{32}P$) Solution*

*Suxamethonium Bromide*

*Tetracycline and Procaine Injection*

*Zinc Undecenoate*

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# AN INTRODUCTION TO PHARMACOLOGY AND THERAPEUTICS

# PREFACE TO THE NINTH EDITION

THE thirty years which have elapsed since the first edition of this book was published have been a period of unparalleled advances in Pharmacology and Therapeutics. The discovery of new remedies has revolutionized the treatment of disease. Research laboratories, academic and commercial, have multiplied the world over, and investigation proceeds with gathering momentum. New chemical compounds are being prepared and pharmacologically tested in their hundreds. Only a very few merit therapeutic trial and still fewer succeed in finding an assured place in medical practice.

The medical practitioner finds it hard to keep up with these rapid and continuous advances. The student beginning the subject is faced with a formidable list of outlandish names with which he must learn to associate pharmacological and therapeutical properties. The writer of an introductory book must discriminate in his choice of material. For this, fortunately, the current editions of the British and United States Pharmacopoeias provide a reliable general guide.

I have been stimulated to revise this little book by requests from teachers and from the Oxford University Press, and in its final completion have had valued help from my old colleague, Dr. J. D. P. Graham. All chapters have been revised and most of them largely rewritten. Some new sections have been added. Of groups of drugs, perhaps the most substantial additions have been made to antibiotics, hormones, autonomic drugs, anaesthetics, analgesics, sedatives, and antihistamines. I hope that as revised the book may continue to fulfil its original purpose.

J. A. G.

*Hermitage, Berks.*
*August 1957*

# PREFACE TO THE FIRST EDITION

DURING the years in which I have had the privilege of teaching medical students in Oxford, I have given a course of lectures dealing with the actions and uses of drugs, supplemented by practical courses in Pharmacology and in Pharmacy. Owing to the increasing demands upon the medical curriculum, this yearly course of lectures has been limited to fifty. Such a course could not give much more than a general sketch of the subject, the student being left to fill in detail from text-books or other sources. Without such a general survey the student is apt to lose himself in a mass of detail and often fails to get any sense of proportion or scheme of classification.

I have often wished to alter this procedure by providing the student with such a short but comprehensive survey in book form as would leave the lecturer more freedom and latitude to deal with more advanced and advancing aspects of the subject. The smaller books that are available do not furnish the desired survey because they achieve brevity by compression rather than by selection and arrangement. I am also frequently asked to recommend a book which a student can read in the vacation before attending lectures, and for this a large text-book is unsuitable.

It is for these purposes that this little book has been written, though I can hardly hope that its sphere of usefulness will be commensurate with the time I have spent upon its compilation.

J. A. G.

*Oxford 1929*

*Were angels to write books, they would never write folios*

OLIVER GOLDSMITH

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# I

# INTRODUCTION

## ORIGIN AND SOURCES OF DRUGS

ALL races of mankind have tried to heal those who suffer from diseases, and of the many curative methods which have been employed, one of the most ancient and successful has been treatment by means of drugs. The drugs which are used medicinally at the present day have been discovered at different times and in different countries. They come from different sources; animal, vegetable, and mineral substances, as well as artificially prepared compounds, have all been pressed into service as remedial agents.

It is not difficult to imagine how, for example, plants came to be used as remedies. Man had to discover which plants were edible and which were not. They bore no labels. In the process of seeking for food, it would be found that some plants produce unusual effects. They might purge, for example, and the step would be a fairly easy one to use such a plant as a remedy for constipation. Some would be found to be powerful poisons, and extracts of these came to be used in some countries, for example, as arrow poisons. Long before there was any science of experimental pharmacology, or even before there was any real knowledge of the causes of disease, a large amount of information had thus accrued of the remedial and toxic properties of plants.

One can imagine also how an elementary knowledge of pharmaceutical processes would arise. A recognition of any unusual action of a plant might result at first from eating a leaf. A leaf stored for future use might crumble, and it would be found that the leaf retained its activity in the form of a powder. If it were cooked, it might be noticed that the active properties of the plant were conveyed to the water in which the plant was cooked, and even to the residue left when the water evaporated. So might come about the employment of plants in the form of a

powder, an infusion, or an extract, methods of preparation which are still in use.

It required a much greater knowledge (in some cases a very modern knowledge) of chemistry to determine which particular constituent of a plant was responsible for its curative or toxic actions, and to determine the chemical nature of this, the 'active principle' as it is called. This kind of knowledge has really been acquired only in the last century. For example, cinchona bark was used as a remedy for malaria for about two centuries before the active principle, quinine, was isolated from it. The active principles of most important medicinal plants are now known, and in some cases their exact chemical composition. Especially in the last fifty years it has become possible with advancing knowledge to use the active principles in place of a crude drug or of extracts from it. The amount of active principle in a plant varies with such factors as the soil in which it grows and the climate. Even if an extract is always made in the same way, therefore, its activity will vary. But the active principle is a definite chemical substance, of unvarying composition and often more stable than an extract, and therefore dosage with it can be more accurate.

One large group of drugs, therefore, consists of plants or parts of them, of extracts made from plants, and of active principles—alkaloids, for example—isolated from plants. Other substances have been used as remedies. Some of these are substances occurring in nature like sulphur, compounds of iron, or salts like Epsom salts. A very important group of drugs has been introduced especially in the last half-century or so, substances which have been manufactured in the chemical laboratory. An early type of such a substance would be alcohol, manufactured by the fermentation of sugar. The important anaesthetics chloroform and ether are artificially made, so are most of the hypnotics, chloral and barbiturates for example. Though plant constituents continue to be investigated with a view to discovering new remedies, an increasing number of new drugs are such compounds artificially synthesized or manufactured in the chemical laboratory.

It follows from this that not only have drugs come to us from different sources and through different channels, but our knowledge of their action and effects has been variously acquired. Drugs were employed in the treatment of diseases long before the pathology of these diseases was understood. The investigation of the pharmacological actions of drugs is a comparatively new science. In the course of time, therefore, various remedial actions of drugs were discovered for which no scientific explanation could, at the time, be given. With the advances in knowledge of physiology, pathology, and pharmacology, especially in the last half-century, these explanations have in many cases been forthcoming. To make a rough classification, our present knowledge of the effects of drugs has been acquired in two ways. Older remedies were discovered chiefly by observing their remedial effects in diseases in man, while the pharmacological basis of these effects has only recently, and as yet imperfectly, been established. On the other hand, substances, artificial or other, which are now for the first time investigated as to their possible value as remedial agents, are first examined, usually on laboratory animals, as to their physiological actions and toxicity, and it is upon the results of this investigation that a possible field for their tentative therapeutic use is based.

*Pharmacology* (Greek, *pharmakon*, a drug) may be defined as the action of drugs on normal animals or tissues. *Therapeutics* (Greek, *therapeuein*, to heal) means, so far as drugs are concerned, their remedial action in the treatment of disease. *Chemotherapy*, a word not precisely defined, generally refers to treatment by means of substances of known chemical composition, as opposed to antitoxins. From the experimental point of view, it differs from pharmacology in that the therapeutic action of a drug is usually investigated in animals infected with a specific pathogenic micro-organism.

The term *Pharmacognosy* is applied to the knowledge of the sources and chemical properties of drugs, while the art of preparing drugs in forms suitable for medicinal administration is called *Pharmacy*.

As a guide to the physician and pharmacist, most countries publish from time to time an authoritative list of drugs in general use with information regarding their sources and physico-chemical properties, doses, &c. It contains also a description of standard 'preparations' of drugs. A most important function of a pharmacopoeia is to lay down standards of composition and purity to which all medicaments used in regular practice should conform. As new drugs are introduced or old ones discarded, this list has to be revised. In this country the book in question is called the *British Pharmacopoeia* and it is published under the direction of the General Medical Council. Amendments to the current edition may be published in an *Addendum*, which has the same authority as the *British Pharmacopoeia*. The latest edition was published in 1953 and the *Addendum 1955 to the British Pharmacopoeia 1953* became official in 1956. Drugs or preparations recognized in this book are called 'official' remedies; or the initials (B.P.) are placed after the name of the drug. Similarly (U.S.P.) stands for the *Pharmacopeia of the United States*, the Fifteenth Revision of which was issued in 1955, (U.S.P. XV), and the first supplement in 1957. Another book, the *British Pharmaceutical Codex* (B.P.C.), published by direction of the Council of the Pharmaceutical Society of Great Britain, gives information mainly about medicaments which, though in fairly constant demand, are not included among official remedies. The current edition was published in 1954 and amendments are given in a supplement which is published between editions, the latest one being June 1957. It includes a large number of formulae and, unlike the *Pharmacopoeia*, descriptions of the actions and uses of drugs. The *British National Formulary 1957* gives a list of formulae useful in general medical practice especially under the National Health Scheme. It gives useful and concise information about the actions of some important groups of remedies. An alternative edition is now available in which the arrangement is on a pharmacological basis, for the use of medical students. The American *National Formulary* covers much the same ground as the B.P.C. *New and Nonofficial Remedies*, issued

annually under the direction of the American Medical Association, gives helpful information about new drugs and their therapeutic values.

## METHODS OF ACTION OF DRUGS AND CONDITIONS INFLUENCING THESE

### LOCAL AND GENERAL ACTIONS

By local action is meant the action which a drug exerts at the site of application and before it is absorbed into the blood stream. This includes not only such obviously external actions as, for example, the action of an ointment on the skin or of a solution applied to the conjunctiva, but also the action of a gargle on the surface of the throat or of a solution used to wash out the bladder. Drugs administered by mouth act first on the surface of the alimentary canal, effects which are included among local actions.

By general action is meant the action of a drug *after absorption*. In this case the drug is carried by the blood to all the tissues in the body, which therefore are all subjected to the same concentration of it. It is found, however, that under these circumstances the different tissues of the body are not equally sensitive to the action of any drug. In other words, drugs have what is called a *selective action* on the tissues. This selective action is more marked with some drugs than with others, but is displayed by them all. Indeed, the possibility of their being used medicinally usually depends upon this. When a dose of 2 milligrams of strychnine is given intravenously to a man weighing 70 kilograms, the concentration in the blood (once it is evenly distributed and before any of it is excreted) is about 1 part in 2 or 3 millions. This concentration may stimulate the central nervous system, but even much larger doses, which would give correspondingly higher concentrations in the blood, have no such effect on other tissues. Extract of pituitary gland is extensively used to stimulate the contractions of the uterus in labour, but it could hardly be used for this purpose if it had an equal effect on the muscle of the bronchi, because in

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