

TOXICOLOGY
Mechanisms and Analytical Methods

VOLUME I



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TOXICOLOGY

Mechanisms and Analytical Methods

Edited by

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VOLUME I

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FOREWORD

Each year there is a sharp increase in the number of potentially poisonous substances to which man is exposed. They are met with in the factories, in the fields, and in the homes. They often contaminate the air, may be present in food or beverage, and are contained in most medicines.

The number of instances of illness and death caused by poisoning as reported in the vital statistics of countries where such figures are compiled probably represents only a small fraction of those which actually occur. Thus, in one large American industrial community a total of 66 cases of lead poisoning were reported over a seven-year period. During the seventh year, the services of an analyst and the facilities of a well-equipped laboratory were made available to the physicians of the community for making urinary lead determinations. At the same time, a program of professional education concerned with the clinical recognition of lead poisoning was launched. The following year, 65 cases were recognized. Since there was no reason to believe that there had been anything like a seven-fold increase in poisoning during that particular year, it was inferred that the apparent increase was due largely to better detection.

Whatever the facts may be as to the frequency with which poisoning actually occurs, it is clear that there is a need in most countries for much better facilities than now exist for securing toxicological analyses as well as for greater alertness on the part of the medical profession in the recognition of poisoning.

The many advances that have been made in the field during the past several decades are widely scattered and relatively difficult to locate. They are to be found in the files of more than a hundred scientific journals, in the many monographs that deal with special analytical methods or with special kinds of poisoning, and in chapters devoted to analytical toxicology that are to be found in various textbooks of legal medicine.

The first reaction on learning the contents of these two volumes, of one whose requirements for knowledge in the field although frequent and diversified are not such as to justify the maintenance of a large special library, is one of great relief. It is to be hoped that these volumes

will stimulate a general interest in this important subject—an interest that will lead to improvement in the recognition and prevention of poisoning and in the care of the poisoned.

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June 17, 1960

PREFACE

The preparation of this work on toxicological analysis was undertaken with the help of a team of collaborators all of whom were thoroughly experienced in this work and were especially interested in a particular phase of it. This method was adopted because it was quickly realized by the editors that the task was beyond the capacity of one or two men, owing to the vast range and rapid growth of the diverse sciences from which the toxicologist must borrow so many of his techniques and so much of the knowledge he needs to interpret his results.

The editors' objective in organizing these volumes has been to supply first an account of the general methods of chemical analysis available to the toxicologist along with a discussion of the principles on which they are based and a survey of the material to which they are to be applied. In pursuance of this aim, an introductory chapter deals with general aspects of the work of a toxicological analyst. This is followed by a series of chapters on the mode of absorption and excretion, the distribution in the body, and the metabolic changes undergone by toxic substances. Knowledge of these subjects, or the means of acquiring it when needed, is an essential part of the armament of the toxicologist—or other medico-legal consultant—since he must know what to look for, where and when his search may be successful, and how his results are to be interpreted with respect to amount of poison administered, the time and route of administration, and other factors of enormous importance in extracting the full value of the chemical analysis. Then follow chapters on methods of extraction, identification, and quantitation, which complete the first volume. The methods of analysis available to the toxicologist are given with sufficient discussion of the principles and sufficient examples of their use to indicate extensions to other particular instances. This is necessary because, since every new drug is a potential poison, the list of substances within the purview of the toxicologist is continually growing longer. Unquestionably, each worker will modify the techniques to suit his specific purpose or study, and the approach used is designed to take cognizance of this rather than to present a series of rigidly standardized procedures.

The main part of the second volume supplements the methods quoted in the first volume as specific examples of general procedures by considering in turn the various important groups of poisons, arranged approximately in their order of extraction from biological material, and bringing together the methods available for identifying and determining

the members of each group. In each of these chapters there are numerous specific examples, but though it was necessary to be selective, enough guidance is given to help in the selection of tests to be tried for new drugs of known chemical composition.

Since the toxicologist should clearly understand something of the nature of toxic action even though he may be primarily an analyst and not a pharmacologist, the second volume is prefaced by a short essay on this subject and this, being of general interest rather than a detailed study, is less fully documented and gives leading references for further reading instead of the full bibliographies which are an important feature of the other chapters. Similarly, because toxicologists are often asked for advice on treatment, a chapter on this subject brings the volume to a close.

It is hoped that this plan will make the treatise valuable to all who may be concerned with the identification and determination of poisons (which in practice may mean any drugs). In this group of scientists are included, besides professional toxicologists, clinical chemists who are inevitably drawn into such work from time to time, and biochemists who as collaborators in pharmacological or medical studies require help in selecting and carrying out analytical procedures.

References to the literature cited are arranged alphabetically (according to authors' names) at the end of each chapter. A separate author index has not been included in the volume since it is felt that the reader will be able to find the material he is seeking by referring to the detailed subject index and the reference lists.

We gratefully acknowledge the help and cooperation of the contributors and the willingness with which they undertook their task. We also wish to think Miss Dorothy E. Carlson and Mrs. Elizabeth Proffitt for their valuable assistance and patience. Finally we should like to express our admiration of the work done by the publishers and printers of the book; their help enormously lightened our burden.

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June 1960

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I. INTRODUCTION

In this introductory chapter we propose to discuss briefly certain aspects of the toxicologist's work which are not restricted to one particular analytical technique but are of general importance.

This book does not detail the clinical symptoms or the pharmacological effects of individual poisons, concentrating rather on the methods of detecting, identifying, and determining toxic substances. It does, however, give a brief general account of modern views on the mode of action of poisons because the practicing toxicologist, even if he is essentially a laboratory worker and not a clinician concerned with the diagnosis and treatment of poisoning, must nevertheless have a sound knowledge of the effects of poisoning. Otherwise he will frequently be unable to make proper use of the information available to him, will waste many hours in unprofitable labor, and may even fail in his task through ignorance of what to look for and where to look for it.