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PHARMACOLOGY AND TOXICOLOGY OF URANIUM COMPOUNDS

Chronic Inhalation and Other Studies

Edited by

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**PHARMACOLOGY AND TOXICOLOGY
OF URANIUM COMPOUNDS**

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FOREWORD

The wartime project for development of atomic energy was a remarkable feat of cooperation and accomplishment by government, science, industry, labor, and the military services aimed exclusively at the military application of atomic energy. Our present national atomic energy program, expanding upon the previous developments, is directed not only toward the assurance of national security but also toward the realization of the immense potential benefits atomic energy holds for our civilization. The record of progress and the results of extensive scientific investigations and engineering development are contained in the National Nuclear Energy Series. This knowledge, which offers the basis of world-wide benefits from nuclear science, is being published in the established scientific tradition, not solely to meet the precise needs of science but also in support of the high goals of the American people set forth in the Atomic Energy Act. The work reported in this series is a tribute to all the scientists engaged in both the Manhattan Project and the postwar Atomic Energy Commission program.

Gordon Dean, Chairman
U. S. Atomic Energy Commission

PREFACE

This volume is one of a series which has been prepared as a record of the research work done under the Manhattan Project and the Atomic Energy Commission. The name Manhattan Project was assigned by the Corps of Engineers, War Department, to the far-flung scientific and engineering activities which had as their objective the utilization of atomic energy for military purposes. In the attainment of this objective, there were many developments in scientific and technical fields which are of general interest. The National Nuclear Energy Series (Manhattan Project Technical Section) is a record of these scientific and technical contributions, as well as of the developments in these fields which are being sponsored by the Atomic Energy Commission.

The declassified portion of the National Nuclear Energy Series, when completed, is expected to consist of some 60 volumes. These will be grouped into eight divisions, as follows:

- Division I — Electromagnetic Separation Project
- Division II — Gaseous Diffusion Project
- Division III — Special Separations Project
- Division IV — Plutonium Project
- Division V — Los Alamos Project
- Division VI — University of Rochester Project
- Division VII — Materials Procurement Project
- Division VIII — Manhattan Project

Soon after the close of the war the Manhattan Project was able to give its attention to the preparation of a complete record of the research work accomplished under Project contracts. Writing programs were authorized at all laboratories, with the object of obtaining complete coverage of Project results. Each major installation was requested to designate one or more representatives to make up a committee, which was first called the Manhattan Project Editorial Advisory Board, and later, after the sponsorship of the Series was assumed by the Atomic Energy Commission, the Project Editorial Advisory Board. This group made plans to coordinate the writing programs at all the installations, and acted as an advisory group in all matters affecting the Project-wide writing program. Its last meeting was held on Feb. 9, 1948, when it recommended the publisher for the Series.

The names of the Board members and of the installations which they represented are as follows:

Atomic Energy Commission Public and Technical Information Service	Alberto F. Thompson
Technical Information Division, Oak Ridge Extension	Brewer F. Boardman
Office of New York Operations	Charles Slessor, J. H. Hayner, W. M. Hearon *
Brookhaven National Laboratory	Richard W. Dodson
Carbide & Carbon Chemicals Corporation (K-25)	R. B. Korsmeyer, W. L. Harwell, D. E. Hull, Ezra Staple
Carbide & Carbon Chemicals Corporation (Y-12) †	Russell Baldock
Clinton Laboratories ‡	J. R. Coe
General Electric Company, Hanford	T. W. Hauff
General Electric Company, Knolls Atomic Power Laboratory	John P. Howe
Kellex Corporation	John F. Hogerton, Jerome Simson, M. Benedict
Los Alamos	R. R. Davis, Ralph Carlisle Smith
National Bureau of Standards	C. J. Rodden
Plutonium Project Argonne National Laboratory	R. S. Mulliken, H. D. Young
Iowa State College	F. H. Spedding
Medical Group	R. E. Zirkle
SAM Laboratories §	G. M. Murphy
Stone & Webster Engineering Corporation	B. W. Whitehurst
University of California	R. K. Wakerling, A. Guthrie
University of Rochester	D. R. Charles, M. J. Wantman

* Represented Madison Square Area of the Manhattan District.

† The Y-12 plant at Oak Ridge was operated by Tennessee Eastman Corporation until May 4, 1947, at which time operations were taken over by Carbide & Carbon Chemicals Corporation.

‡ Clinton Laboratories was the former name of the Oak Ridge National Laboratory.

§ SAM (Substitute Alloy Materials) was the code name for the laboratories operated by Columbia University in New York under the direction of Dr. H. C. Urey, where much of the experimental work on isotope separation was done. On Feb. 1, 1945, the administration of these laboratories became the responsibility of Carbide & Carbon Chemicals Corporation. Research in progress there was transferred to the K-25 plant at Oak Ridge in June, 1946, and the New York laboratories were then closed.

Many difficulties were encountered in preparing a unified account of Atomic Energy Project work. For example, the Project Editorial Advisory Board was the first committee ever organized with representatives from every major installation of the Atomic Energy Project. Compartmentation for security was so rigorous during the war that it had been considered necessary to allow a certain amount of duplication of effort rather than to permit unrestricted circulation of research information between certain installations. As a result, the writing programs of different installations inevitably overlap markedly in many scientific fields. The Editorial Advisory Board has exerted itself to reduce duplication in so far as possible and to eliminate discrepancies in factual data included in the volumes of the NNES. In particular, unified Project-wide volumes have been prepared on Uranium Chemistry and on the Analysis of Project Materials. Nevertheless, the reader will find many instances of differences in results or conclusions on similar subject matter prepared by different authors. This has not seemed wholly undesirable for several reasons. First of all, such divergencies are not unnatural and stimulate investigation. Second, promptness of publication has seemed more important than the removal of all discrepancies. Finally, many Project scientists completed their contributions some time ago and have become engrossed in other activities so that their time has not been available for a detailed review of their work in relation to similar work done at other installations.

The completion of the various individual volumes of the Series has also been beset with difficulties. Many of the key authors and editors have had important responsibilities in planning the future of atomic energy research. Under these circumstances, the completion of this technical series has been delayed longer than its editors wished. The volumes are being released in their present form in the interest of presenting the material as promptly as possible to those who can make use of it.

The Editorial Advisory Board

UNIVERSITY OF ROCHESTER PROJECT FOREWORD

The inception and the organization of the University of Rochester Atomic Energy Project, which operated under the name University of Rochester Manhattan Project during the war years, were described by the former Director, Dr. Andrew H. Dowdy,* in the Foreword to Parts I and II of this volume. Postwar changes have included the development of a postgraduate educational program in medical and biological fields of interest to the Commission. At the present time, this includes about 80 students in Health Physics, Radiation Biology, Biophysics, Pharmacology and Toxicology, and Industrial Medicine. In keeping with this trend, the Department of Radiation Biology of the School of Medicine and Dentistry was organized in January, 1948, to administer the Project under contract with the Atomic Energy Commission and to integrate the teaching activities with those of the rest of the School.

The research program continues to be devoted principally to the solution of health and medical problems arising from atomic energy development in the facilities of the Commission and its contractors. This includes studies in the broad fields of the toxicity of both radioactive and nonradioactive materials, the biological effects of radiation, therapy against radiation injury, flash burns, and instrument and method developments in these fields.

Henry A. Blair
Head of the Department of
Radiation Biology and Director
of the Atomic Energy Project
University of Rochester

May, 1952
Rochester, N. Y.

* Present address: Medical School, University of California at Los Angeles.

VOLUME EDITOR'S PREFACE

Parts III and IV of this volume are concerned chiefly with two kinds of information: (1) the chronic inhalation toxicity of uranium compounds and (2) the mechanism of uranium poisoning. In Parts I and II the results of the short-term studies are presented; these serve as the basis for the chronic toxicity tests. It is most appropriate, therefore, to retain the same title for the entire presentation. Because Parts III and IV were not planned when the original sequence of the National Nuclear Energy Series volumes was arranged, many complications arose. The decision to present these results as Parts III and IV of the "Pharmacology and Toxicology of Uranium Compounds" was a difficult one for the McGraw-Hill Book Company to make, but a decision that has been gratifying to us.

Yearlong inhalation experiments have been carried out using four uranium compounds; in addition, there was a single 2-year study of animals breathing atmospheres containing soluble or insoluble uranium compounds for 1 year and then breathing uranyl nitrate dust for the second year. An extensive experiment is described in which animals were given uranium compounds by insufflation. Feeding tests of 2 years' duration using rats and of 1 year's duration using dogs provide the necessary correlative data.

Mechanism studies are directed toward two major problems: (1) the bone deposition of uranium and (2) the inhibition of carbohydrate metabolism by solutions of hexavalent uranium. The contributions that these studies make to our knowledge of the normal processes of calcification and of cellular metabolism should be stressed.

Additional work is included on tolerance to uranium poisoning, on the chemical complexing of uranium in the body fluids, and on the modes of pulmonary retention of particulate matter. A partial bibliography, more complete than any previously available, of the biological effects of uranium compounds is given in Chap. 27 under two headings: (1) effects on plants and (2) other references. A few analytical methods not given in Chap. 2 are presented. Additional toxicology data concerning certain fluorides (a continuation of Chap. 17) are described.

Dr. Carl Voegtlin wrote in the Volume Editor's Preface to Parts I and II, "It is fair to say that the study of the toxicology of uranium compounds herein described represents the most comprehensive ex-

perimental investigation of an industrial poison ever carried out by any group of scientific workers in such a short time." Dr. Voegtlin had in mind also the investigations reported in Parts III and IV, especially the chronic tests and the work on mechanism, both of which were completed some months after Parts I and II were written. It is my privilege to acknowledge the contributions made by Dr. Voegtlin to every part of this project and to mention the personal price he paid. As he retired from the Public Health Service in July, 1943, Dr. Voegtlin looked forward with great anticipation to quiet years of research in his special field, the chemistry of cancer, in one of the several university laboratories proffered him. Instead, unhesitatingly and with complete selflessness, he put aside cancer research for three years to "do his bit" in the Manhattan Project.

The completion of these studies has made possible the well-supported recommendation of air concentrations of soluble and insoluble uranium dusts—maximal allowable concentrations—that men may breathe safely. Providentially, this highly toxic metal is not easily absorbed. The studies in Parts III and IV present the evidence.

Harold C. Hodge

May, 1952

Rochester, N. Y.

The Manhattan Project Technical Section of the National Nuclear Energy Series is intended to be a comprehensive account of the scientific and technical achievements of the United States program for the development of atomic energy. It is not intended to be a detailed documentary record of the making of any inventions that happen to be mentioned in it. Therefore, the dates used in the Series should be regarded as a general temporal frame of reference, rather than as establishing dates of conception of inventions, of their reduction to practice, or of occasions of first use. While a reasonable effort has been made to assign credit fairly in the NNES volumes, this may, in many cases, be given to a group identified by the name of its leader rather than to an individual who was an actual inventor.

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CHRONIC STUDIES

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