Toxicology of Insecticides

By Fumio Matsumura

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Preface

Why are books written? Since I have read many works by my colleagues with admiration, this question has always intrigued me. Further, writing a book takes a good deal of time and effort, and I had imagined that I would never undertake such a demanding task. A few unexpected events and circumstances have changed my mind. The first was the pleasant experience of editing *Environmental Toxicology of Pesticides* with Drs. Mallory Boush and Tomomasa Misato. This fine symposium volume occasioned many interesting responses, including a suggestion to prepare a more complete treatise on the grounds that such "proceedings" volumes, by their very nature, do not satisfactorily offer a complete and coherent description of the field, but cater chiefly to specialists. I myself prefer single-authored books for basic understanding of a scientific field.

The second circumstance leading to the present volume was the availability of teaching notes from my course on the toxicology of insecticides. As the need to cultivate environmental awareness has increased, there has been a parallel increase in the enrolments of such courses both here and in other major institutions. Yet no comprehensive and up-to-date text has been available. The third factor which facilitated the effort was an especially pleasant sabbatical in Hawaii, where the availability of the excellent Hamilton Library at the University of Hawaii considerably eased my task.

The problems I confronted were mainly related to the scope of the field, the scarcity of sufficiently solid results in certain areas to warrant clear-cut conclusions (particularly in the field of environmental toxicology), and, more seriously, the necessity to provide coverage of the exceedingly diverse areas that contribute to research on insecticide toxicology. In each case, certain compromises were necessary to complete my original intentions.

The book that resulted then is designed for use by graduate students and the general scientific community rather than those already expert in the field. It is my intention that the volume be self-contained so that the reader can rapidly develop an understanding of the basic ideas of the field. The fundamental references and related material are amply documented for those who wish to study any aspect further.

To review and digest this colossal amount of information posed another problem. Because I have experienced disappointments with computer searches of the literature, I have relied solely on customary search methods, and trust I have missed no important papers. I have also taken the liberty of freely borrowing data from existing books and reviews for the chapters covering well-established fields (e.g., Chapter 3, on the characteristics of insecticides) and have collectively listed those useful references at the beginning of each chapter to clarify the source of information. They were most helpful in summarizing and extracting principles, and I would like publicly to thank their authors here.

Finally, I want to offer briefly my philosophy on pesticide pollution. In this treatise I wanted to examine all possibilities, even if it meant being scientifically risky or remote. This position derives from the special circumstance that problems in the environment are seldom discovered unless one specifically looks for them. The difficulties we confront with PCBs, dibenzodioxins, methyl mercury, etc., remain most refractory, and all point to the necessity of imaginative and daring approaches. My discussion of carcinogenicity and mutagenicity, for example, reflects such a view. On the other hand, I have also tried to critically examine the validity of all such unproven claims and hypothesis. Wherever possible, I avoided comparison of unrelated works, and instead relied on data which clearly are scientifically sound and repeatable. For instance, in arriving at a conclusion on the role of biomagnification in environmental toxicology, I relied on bioaccumulation data taken from the limited ecosystems where the history of contamination is known, thus avoiding unwarranted comparisons between fish from Santa Monica Bay and North Atlantic sea birds.

The book could not have been completed without the help of Ms. Claudia T. Ward, who diligently assisted me in detailed editorial matters.

I would also like to thank Dr. Wallace C. Mitchell and other staff members of the Entomology Department, University of Hawaii, for arranging my stay and the use of the library facilities.

I further thank the authors and publishers of numerous references for permission to reproduce figures which helped immensely to illustrate scientific principles.

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Introduction

1.1. TOXICOLOGY

Toxicology is one of the oldest branches of pharmacology. Traditionally, it has been thought of as the science of poisons affecting human lives and, therefore, as a branch of medical science. DuBois and Geiling (1959) provided the following definition: "Toxicology is that branch of medical science that deals with the nature, properties, effects, and the detection of poisons. It is, therefore, the science of poisons." In this definition are included studies on the metabolism and excretion of poisons, on the action of poisons, and on the treatment of poisoning as well as systematic chemical and physical analyses and diagnoses (Stewart and Stolman, 1960).

In recent years a branch of this subject, now known as environmental toxicology, has grown increasingly important. Its development has been fostered, even necessitated, by (1) the extensive use of industrial chemicals, pesticides, and natural resources, (2) more intense utilization of urban, agricultural, and recreational space and marine environments, and (3) heightened awareness of the hazards of chemicals to wildlife, domestic animals, and people.

All this constitutes quite a departure from the traditional concerns of toxicology, since in the past the principal emphasis has been on human subjects and domestic animals. Until quite recently, for instance, the most important subfield of toxicology was industrial toxicology (DuBois and Geiling, 1959), which is concerned mainly with the safety of industrial workers and, to a much lesser extent, with that of other people who might accidentally be exposed to large doses of industrial poisons. Under the rubric of environmental toxicology, the domain of toxicologists has been enlarge-

to incorporate all forms of biological systems including wildlife, man, and domestic animals. Studies on metabolism, transport, translocation, physicochemical transformation, etc., have been expanded to include the entire spectrum of ecosystems, physical environments, the biosphere, and even the total environment on a global scale. Despite these roots, however, environmental toxicology is an entirely new discipline. Its history dates back to 1962, the year *Silent Spring*, the famous book by Rachel Carson, appeared. Its scope and principles are not yet clearly defined (see preface in Matsumura *et al.*, 1972), although ultimately its natural evolution as a scientific discipline will resolve this problem. In the present chapter, I shall attempt to explain its background and my own view of the field today.

The biocidal agricultural chemicals, collectively known as pesticides, are, without any question, the largest group of poisonous substances that are widely broadcast today. Pesticides include insecticides, acaricides, nematocides, rodenticides, herbicides, and fungicides. Insecticides (in the broad sense, acaricides and nematocides are included) are the most numerous and most valuable pesticides. As in the case of many other biologically active substances, insecticides have been developed mostly by empirical methods, notably by screening countless numbers of compounds that kill the pest organisms, and not by logical considerations of their properties and the consequences of their use. The necessity to use insecticides properly forced entomologists to study their properties, since far greater knowledge of the nature of insects as well as of the problems of insect pests in agriculture and public health was required.

Insecticide toxicology differs from its parent discipline, medical toxicology, in that it does not include clinical diagnoses or treatment of human patients who are affected by insecticides; however, insecticide toxicology does include efforts to determine tolerance levels of pesticides in man and is concerned with establishing a logical basis for selective toxicity, in order to kill insects without affecting mammals. In this connection, there is an overlap between insecticide toxicology and veterinary toxicology, since the latter is often devoted to studies of the effects of various pesticides on domestic animals. Radeleff (1964) describes the field by saying, "A veterinary toxicologist, then, may be considered to be a veterinarian having a special knowledge of the poisons affecting the mammals and birds in which man is interested for his economic gain or personal pleasure, and of those substances which, when present in animal products, could be harmful to the people who may consume them." In other words, veterinary toxicologists are concerned with any toxic substance that may come in contact with domestic animals just as medical toxicologists are concerned with the effects of poisons on humans, and these poisons include pesticides.

Insecticide toxicologists, on the other hand, are interested in *any* organism that may be affected by insecticides, not in the welfare of insects (even though in many university departments of entomology their section is somewhat confusingly called "insect toxicology"). They are concerned with the elucidation of the mechanisms of action of toxicants and with the differences in their inhibitory action and metabolic fate in various organisms, which may then provide an understanding of their differential toxicities. In other words, insecticide toxicology is a discipline based on the study of a particular group of toxic chemicals rather than on their effects in a particular group of animals.

Environmental toxicology is a very broad discipline. The field can be subdivided according to the compounds and materials involved: that is, the environmental toxicology of pesticides, or of industrial pollutants, or of insecticides, or of microcontaminants. However, environmental toxicology is also organized along the lines of medical toxicology in that it is concerned with the effects of poisons on a particular group of "patients"—the various ecosystems of the environment. This new field has attracted scientists from wildlife ecology, pesticide toxicology, pharmacology, medical (including industrial) toxicology, water chemistry, analytical chemistry, food science, soil science, and many other interdisciplinary fields. Environmental toxicology is thus a hybrid of a wide variety of scientific disciplines; it requires of its practitioners solid fundamental knowledge of chemistry, biochemistry, physiology, and pharmacology, and, when necessary, competence with physical, mathematical, ecological, and other techniques which toxicologists employ to solve problems.

Two factors are important in defining the field of environmental toxicology of pesticides. First, among environmental pollutants pesticides are unique in that they are present in such minute quantities, and, second, their effects are confined exclusively to biological systems. Thus, whatever his initial training, an environmental toxicologist, and particularly an insecticide toxicologist, must sooner or later be trained in the knowledge of poisons and must have an interest in learning how such low levels of insecticides interfere with living systems and how living organisms react to these chemicals. It is crucially important to study how animals are poisoned by insecticides and why they die, and this knowledge must then be utilized in assessing environmental impact.

1.2. GENERAL PATTERNS OF PESTICIDE USE

Table 1-1 is a summary of pesticide production in the United States during the period 1966 through 1969. Insecticides account for roughly

TABLE 1-1. Total Organic Pesticide Production Figures for the United States (in millions of pounds)

Pesticides	Year			
	1966	1967	1968	1969
Total fungicides	178.9	177.9	190.8	182.1
Total herbicides	272.0	348.3	402.8	371.8
2,4-D and 2,4,5-T	90.6	110.9	136.7	68.6
Total insecticides	562.2	503.8	582.6	579.5
Cyclodiene insecticides	130.5	120.2	116.0	107.3
Calcium arsenate	2.9	2.0	3.4	2.0
DDT	141.3	103.4	139.4	123.1
Dibromochloropropane	8.7	5.2	7.9	8.6
Lead arsenate	7.3	6.0	9.0	7.0
Methyl bromide	16.3	19.7	20.5	20.0
Parathion	35.9	33.3	38.2	50.6
Other organic insecticides	199.8	202.6	227.3	260.9

From *The Pesticide Review*, 1970 (USDA, 1971).

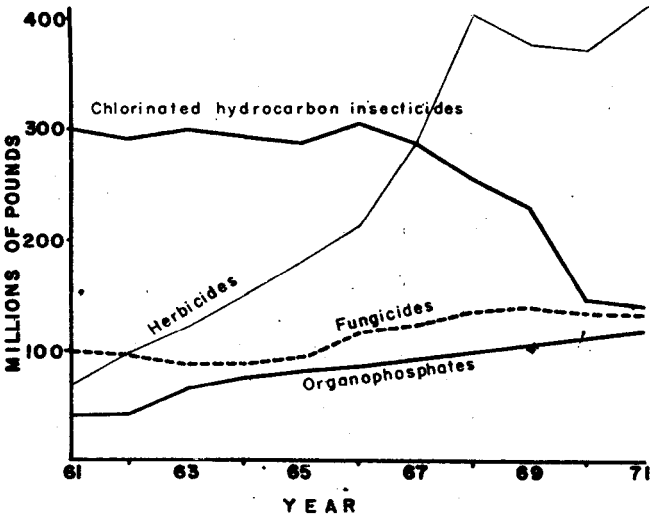

Fig. 1-1. Total production of pesticides in the United States, expressed as millions of pounds per year. Originally from Kearney *et al.* (1969). Amounts since 1967 have been added to update the figure.