TOXICOLOGY OF INSECTICIDES*

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The Toxicology Section of the Technical Development Services was officially begun on July 1, 1949, although a few studies were started in the early spring of 1949. Its purpose is to make a general investigation of the toxicology of economic poisons. The public health aspects of the problem involve: (a) employees in manufacturing and formulating plants, (b) workers or others exposed to pesticides by agricultural uses or in disease-vector control programs, (c) persons occupying treated premises, (d) the general public who consume residues of economic poisons on or in foods, and (e) persons – often children – exposed entirely through carelessness or accident.

The health of employees of industrial plants is the special responsibility of industrial hygienists and is not, therefore, a responsibility of the Technical Development Services. On the other hand, a direct responsibility of the Communicable Disease Center is the health of spray crew operators or of pilots who disperse insecticides as a part of the Center's operational programs. The exposure problem of many agricultural workers essentially is identical to that of the Center's operational field personnel. Unlike industrial workers, they cannot be protected by elaborate or heavy equipment. Even protective clothing or a respirator may prove a burden. Again, persons occupying premises treated for disease-vector control are a responsibility of the Center insofar as their health may be affected by the pesticides used. The study, particularly from the clinical aspect, of the hazard presented by poisonous residues on or in food is a long-recognized duty of the Public Health Service. Although accidental poisoning is a difficult problem to attack, much may be accomplished by widely distributed information. Furthermore, the possibility of poisoning, either accidentally or otherwise, poses the challenge to discover specific antidotes and devise better treatments.

The entire first year of work of the Toxicology Section was devoted largely to a study of the insecticide dieldrin. When this study began, the use of dieldrin in the field was being held in abeyance because so little was known of its toxic hazard to spray workers that it could not be adequately field-tested, much less be recommended for control operations. During that year some work also was done on the possible hazard to occupants, of the residual sprays of chlordan used to treat their houses. The work in toxicology is being expanded into the broader public health field. A project is now being inaugurated to study the problem of toxic residues of insecticides on food.

METHODS

The work of the Toxicology Section is divided into four main approaches: (a) laboratory studies, (b) investigations of operator exposure, (c) clinical studies of human cases of poisoning, and (d) information service. These four approaches are generally applicable to all of the problems undertaken. A brief discussion of these problems will be followed by a short account of work that already has been done.

Laboratory work involves animal exposures by various routes to determine the nature of clinical signs and the variation that may be expected between individuals or between species, and to obtain leads on the mode of action of the poison under study. Once animal exposure has been standardized, antidote studies are begun to see if illness and death caused by the compound may

*For information pertaining to warfarin, a rodenticide, see CDC Bulletin, August 1950, and page 17 of this Bulletin.
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be alleviated by proper treatment or specific medication. To aid in these antidote studies and to serve as a general basis for other work, studies on the pharmacology and biochemistry of the compound are conducted. Chemical studies are required both to determine very minute quantities of a variety of poisons in the various body tissues and to study the normal metabolic processes which may be affected directly or indirectly by the poisons. To aid in the pharmacological and chemical studies, a radioactive tracer laboratory has been established. Finally, pathological studies are made of animals which die or are sacrificed after an experimental procedure.

Field studies of the exposure of spray operators have been necessary because so little is known of the hazard to which these people are subjected. In the course of spraying for either agricultural or public health uses, the operator is exposed to an invisible but continuous rain of small droplets of the spray formulation. These droplets fall on the clothing and the exposed skin, and they may also be inhaled if the particle size is sufficiently small. Such exposure is in addition to any gross accidental contact with the spray formulation of which the operator may be aware. Methods have been developed to sample the fine spray mist contacted by experienced workers under actual field conditions.

Human cases for clinical study may be divided into three classes: (a) persons who are clearly poisoned by an insecticide formulation, (b) persons who are suspected of being poisoned but whose true diagnosis is in doubt, and (c) persons with no apparent illness and no complaints who have had long and extensive exposure to one or more of the compounds under study. Persons in the first group are of particular interest for determining the human symptomatology of poisoning and as test subjects for the most promising forms of treatment developed in the laboratory. It is considered important to study illnesses in which the possibility of poisoning exists since some of these cases eventually prove to be genuine instances of poisoning, thus broadening our knowledge of the nature of poisoning in man. Some forms of illness – for example, headache and subjective dizziness – are difficult or impossible to demonstrate in animals; yet they are quite real and may cause patients great discomfort. Other cases of suspected poisoning eventually prove to be completely unrelated diseases. However, study of such cases of suspected poisoning is not wasted even from the standpoint of toxicology, for if allowed to go misdiagnosed they may eventually cause the limitation of a useful and actually completely safe compound. It also is considered desirable to study persons with extensive exposure to insecticides in order to obtain the earliest possible indication of any adverse effect which may develop. Such examination protects not only the individual who is tested but also other workers who are similarly exposed and, eventually, the whole public who may daily consume minute amounts of the same poison that the worker encounters in relatively large amounts.

The Toxicology Section has been designated as an information center in the Public Health Service on the subject of the hazards of economic poisons where the problem is not one of industrial hygiene. Many letters are received from physicians, public health officials, and the public generally. Some of the questions have to be answered individually, but many answers are contained in a series of clinical memoranda issued by the Technical Development Services.

RESULTS

In the studies on dieldrin, it was found that concentrates are very hazardous and that one might be injured by spillage of even a small quantity. On the other hand, it was shown in extensive animal experiments that repeated exposures to the dilute emulsions used for actual spraying might be tolerated for long periods. The beneficial effect of immediate washing even after gross skin contamination was demonstrated but it was shown that washing is useless if delayed. A comprehensive description of the clinical signs of poisoning was obtained to aid in the diagnosis of possible human cases. Considerable success was obtained in the treatment of dogs and monkeys brought to violent convulsion by an amount of dieldrin which was uniformly fatal to control animals. On the basis of laboratory studies, it was thought safe to carry on limited field tests. The health of workers on these projects was carefully followed and no injury was observed. On the basis of all of the studies in the laboratory and in the field, it has been possible to release dieldrin for the use of governmental agencies and other trained control units for outside residual spraying aimed at the control of disease vectors.

Some of the other commonly used insecticides, including DDT, lindane, chlordan, and aldrin, have

been studied chiefly for the purpose of comparing them with dieldrin. However, these studies have also been an aid in developing antidotes. The study of aldrin was made for the specific purpose of studying the hazard of that compound in floor wax intended for ordinary household use.

Some insecticides give off an appreciable vapor when they are applied as a residual spray, thus acting concurrently as a space treatment. Extensive studies have been carried out on the possible hazard which chlordan may present when used in this way inside of dwellings.

THE STATUS OF FLY RESISTANCE TO INSECTICIDES IN THE SAVANNAH AREA AND ITS IMPLICATIONS IN THE GENERAL PROBLEM OF FLY CONTROL

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The development of resistance to DDT by house flies was first reported in Italy in 1948. At least some of the numerous complaints concerning the lack of effective fly control with DDT in this country in 1947 and 1948 were undoubtedly due to fly resistance, although that fact was not generally recognized at the time. By the early spring of 1949, however, the existence of DDT-resistant strains of house flies in many localities of the United States had been recognized and proved by both laboratory and field tests. Studies were immediately begun by several research agencies to develop DDT substitutes and to study the possible development of resistance to these other potential fly insecticides.

The area in and around Savannah, Ga., is one of the locations where DDT and other halogenated hydrocarbon insecticides have been used for the longest continuous period of time. The Savannah laboratory of Technical Development Services began testing DDT for fly and mosquito control in this area in 1944, with numerous homes and some dairies being treated that year. The following year, 1945, the fly control studies were extended to include not only dairies, but also restaurants, abattoirs, food processing plants, garbage dump areas, and other similar fly foci. These studies were continued on about the same scale in 1946 and 1947, with chlordan also being used on several premises. The Bureau of Entomology and Plant Quarantine of the U. S. Department of Agriculture also used some of the dairies near Savannah for fly control studies in 1945, 1946, and 1947.

A review of the work conducted in 1947 indicates that the results obtained with DDT that year, while still reasonably good, were not as striking as in previous years at the same location. As stated previously, these poorer results were quite likely attributable to the development of fly resistance, but it was not recognized as such at the time; and other reasons, notably poor sanitation, were considered the important causes of the reduced effectiveness.

During 1948, neither the Technical Development Services nor the U. S. Department of Agriculture conducted fly control field experiments with residual sprays in the Savannah area. However, the operators of the dairies and other establishments

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