

# PESTICIDES AND THE FOOD SUPPLY

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(Received for publication February 17, 1966)

## SUMMARY

The use of chemical pest control agents undoubtedly constitutes a calculated risk; nonetheless, the proper use of these agents results in benefits which, at the present time, far outweigh the known potential hazards. Considerable care must be exercised in the selection, storage, and use of pesticide chemicals and in the disposition of the empty containers. Since virtually all pesticides are more or less toxic to man and cumulative and potentiation characteristics are not well defined, regulation through registration and the establishment of residue tolerances is essential. Scientists recognize that the adequate production and preservation of food and fiber and the protection of human health require the use of chemical pesticides. Federal, state, and local health agencies and the food and chemical industries are striving through research and residue surveillance to show the effect of pesticides on human beings and to provide alternative means of pest control. Until these chemical agents are replaced by less toxic means of control, the use of pesticides will continue. As in any scientific venture, the benefit-hazard ratio in the use of pesticides may never be completely established, but we must act on the best available evidence.

The production of an abundance of high-quality nutritious food for mankind has always had its share of problems. For many years, these were essentially microbiological in nature and were concerned with production and processing sanitation to prevent spoilage and foodborne illness. Recently, however, the increased use of chemicals in agricultural practices has resulted in a new problem—residues in food.

The publication *Silent Spring* (9) focused attention on pesticides—their beneficial and harmful characteristics; their effects on the balance-of-nature, the fish and wildlife population, the food supply, and domestic animals; and their total impact on man. Many questions were posed, but they could not be answered with any degree of accuracy. Consequently, to the concerned and confused public, the problems associated with pesticides became as important as those of antibiotic residues in milk, radionuclides in food, the relationship of animal fat to cholesterol level in man, and community air and water pollution.

Although recent papers in the scientific literature have called attention to the general environmental problems associated with pesticides (10 36, 56), a re-

view of the food phase of the problem is appropriate (8) since about 90% of man's pesticide intake is through the food chain.

## CLASSIFICATION OF PESTICIDES

Pesticides may be classified in terms of use and as chemical compounds. Pesticides used to control insects are referred to as insecticides; similarly, rodenticides are used to control rats, mice, and other rodents; herbicides, to destroy unwanted vegetation; soil sterilants, to destroy undesirable plant seed and insect life in the soil; fungicides to prevent and control plant diseases; and fumigants to prevent and control insect and like infestations in stored grain.

Pesticides are chemically classified as chlorinated hydrocarbons, organic phosphates, carbamates, miscellaneous organics, and inorganic compounds. These classifications often signify little in terms of use since a compound may be employed to control several kinds of pests. Literature is available on the chemical composition and classification of pesticides both from manufacturers' and government agencies (23, 42, 81).

## SALE AND USE OF PESTICIDES

By 1964, more than 60,000 formulations, representing approximately 900 chemical agents, had been registered for use in the United States, and the estimated sales of synthetic organic pesticides by primary producers amounted to about \$426 million (75).

Actual figures are not available for other pesticides, but the total supply is estimated at about \$500 million with a gross weight of about 1 billion pounds (75). DDT was the most commonly used pesticide and accounted for 12.4% of the total production.

## REGULATION AND CONTROL OF PESTICIDES

The United States Department of Agriculture (USDA) is responsible for the control of pesticides under the authority of the Federal Insecticide, Fungicide, and Rodenticide Act. The Food, Drug, and Cosmetic Act assigned the responsibility for safety of foods to the Department of Health, Education, and Welfare (DHEW) and the Secretary thereof delegated this responsibility to the Food and Drug

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Administration (FDA). An interdepartmental agreement was formalized in April by the USDA, Department of Interior (DI), and DHEW to coordinate their activities relating to the registration of pesticides and the establishment of tolerances (22). Although the USDA retains administrative responsibility for the Federal registration of pesticides, the FDA and the Public Health Service (PHS), of the DHEW, and the DI are charged with joint responsibility for the review of applications for pesticide registration with regard to their safety for man, fish, and wildlife, prior to registration by the USDA.

To be sold in interstate commerce, a pesticide must be registered with the USDA. In applying for registration, the manufacturer must submit information about the product as to intended use, efficiency of use, directions for use, chemical composition, and toxicological data (77). If, on the basis of data submitted, the USDA finds that no residue remains on food, the pesticide will be registered on a "no residue" basis. If the pesticide does leave a residue and is proposed for use on food crops and animals, the manufacturer must file a petition for tolerance with the FDA, in addition to the application for registration with USDA. This petition must present additional data on toxicity, the tolerance requested, evidence that proper use of the pesticide will not leave a residue in excess of the tolerance, and description of an analytical method for detecting the pesticide at the tolerance level. The FDA can then establish a tolerance on crops or animals as petitioned, whereupon the USDA will grant registration of the pesticide. Registration of the pesticide and establishment of tolerances do not preclude future review and change (77). Each registration must be renewed every 5 years. Official FDA tolerances for raw agricultural products are published annually (58).

Tolerance levels are normally set at 1/100 of the amount found to produce toxicity symptoms in experimental animals, but never higher than necessary to accomplish pest control according to the recommended use of the pesticide. If a compound is found too toxic to permit a residue, the FDA will establish a "zero tolerance" (77). Both "no residue" and "zero tolerance" are modified as analytical methods become more sensitive (77). One example of this is the "zero tolerance" in milk. For practical purposes FDA had previously considered the "effective zero", or actionable level, to be 0.1 ppm of DDT in whole milk, simply because 0.1 ppm was the lower limit of detection of the official method of analysis (1). More recently FDA has stated that in the future any milk containing 0.05 ppm, or above, of DDT, or 0.01 ppm, or above, of any one of a number of other chlorinated hydrocarbons, such as

dieldrin and endrin, would be subject to seizure (16).

Because of its unique position in the feeding of infants, the elderly, and the sick, milk is not considered in the broad category of raw agricultural products. While tolerances as high as 10 ppm have been set for many pesticide residues on various fruits and vegetables, milk and its products are currently required to have a zero pesticide residue concentration. Considerable controversy has occurred as a result of the zero requirement for milk. The Food and Nutrition Board of the National Academy of Sciences (NAS) has recommended that a reasonable tolerance for pesticides be considered in milk (77), and the FDA has stated that they will consider petitions to set tangible tolerance levels in milk for any pest control agent (46).

Recently the "no residue" and "zero tolerance" concepts have been studied by a committee sponsored by the NAS. Although no immediate changes are anticipated, this committee has recommended changes in the basic considerations in the registration and regulation of pesticide chemicals. The most pertinent of these changes involves the abandonment of "no residue" and "zero tolerance" in favor of the more readily definable terms, "negligible" and "permissible" residue levels (63).

#### NECESSITY FOR CONTROL

The mere fact that food and drug laws treat pesticide residues as food adulterants is reason enough to consider such products objectionable. Pesticides, moreover, are not only necessarily toxic to the pests they are intended to control, but many of these agents are also toxic to man and warm-blooded animals. The toxicities of the various pesticides have been studied extensively (2-5, 13, 30, 33, 35, 62, 82). Admittedly, these compounds are quite toxic at high concentration or dosage levels. Some examples of accidental or intentional misuse of pesticides causing illness or death as reported in the literature are the accidental ingestion of relatively large quantities of pesticides by children, excessive exposure of applicators to dusts and sprays through both ingestion and absorption, careless handling of pesticides, thoughtless disposal of the so-called "empty" containers, and intentional poisonings or suicides (14, 24, 25, 32, 38, 41, 55, 57, 67, 85). In the absence of long-term toxicity studies, it cannot definitely be said that the minute residues normally found in contaminated food, are harmful to man. Actually there is evidence to the contrary (34, 87). However, of most concern is the less obvious, more subtle and potentially cumulative effect of low-level, long-term exposure of man to the various pesticide chemicals, individually and collectively (20, 66). These effects

assume a status of more importance when certain characteristics of chemical pesticides are considered.

Chlorinated hydrocarbons are fat-soluble, and most of them tend to accumulate in the fatty tissue of man and animal. The extent of such accumulation and the danger therefrom over a long period of time is not known. DDT and perhaps many other pesticides are rather universally distributed in nature as evidenced by their presence even where applications have probably not been made (70). DDT and DDE concentrations in human body fat in Canada have been estimated to be 3.1 to 7.6 and 7.7 to 20.4 ppm, respectively (64). Estimated DDT in the body fat of the general population in the United States averages about 12.0 ppm, while that of residents of England and Germany is considerably lower (77). These data may reflect—differences in food consumption habits in these countries, since it has been shown that in the United States abstainers from meat retain about half as much DDT as that retained in the general population (34). More recent data, accumulated from a somewhat larger population, indicate a slightly lower DDT concentration in human body fat in this country (37). DDT once stored in the body fat is metabolized and released very slowly, as shown by Huddleston, et al. (39). These investigators found that dairy animals feeding on pasture that had been given a single application of 2 pounds of DDT spray per acre initially secreted milk containing 3.77 ppm and, at the end of 1 year, produced milk containing 0.53 ppm (39). These data have been validated for both milk and meat by Kartashova (43) and Gannon, et al. (26). Recent studies indicate that other chlorinated hydrocarbon insecticides are metabolized in a similar manner (29).

Organic phosphate and carbamate pesticides are generally metabolized by both man and animal into compounds that are currently believed to be relatively nontoxic. Although none of the organic phosphate pesticides appear to remain as such in man or animal for any appreciable period of time, absorption of these agents is probably more hazardous than ingestion. Studies indicate that the poisoning of pesticide applicators by organic phosphates is usually through adsorption (31). Residues of certain of these agents have been found in milk as a result of ingestion by the animals; however, more persistent residues in higher concentrations have been found to result from dusting and spraying of animals (11, 61, 65).

Certain combinations of organic phosphate insecticides have exhibited the characteristic of potentiation or synergistic action (60). This phenomenon results in a much more pronounced effect than could be explained by the additive effects of the two or more individual agents. Potentiation has been re-

ported to result from interference by one of the agents involved with the normal metabolism and detoxification of the other compound or compounds (17). Thus, intoxicating activities of the additional compound or compounds are allowed to proceed more or less uninhibited. Synergistic action may occur among other chemical species of pesticides or perhaps between pesticidal agents and other environmental chemicals, as indicated by observations with carbamate insecticides and organic thiocyanates (18). Consequently, although the consumption by human beings of drugs and other chemical entities together with pesticide residues in food may not be cause for great concern, such relationships are certainly a fertile area for concentrated investigation.

Whether or not synergistic action occurs among chlorinated hydrocarbon pesticides has not yet been established. Early investigations by insect bioassays of combinations of these agents produced conflicting data (77). Recently it has been shown that the concentration of dieldrin in rat tissue decreased in direct proportion to the amount of DDT contained in the DDT-dieldrin supplement fed to the rats (69). Such data may suggest an antagonistic action between these agents.

Decomposition of pesticides by the metabolic activities of man and animal might be responsible for a portion of the acute toxicity and the more subtle potential effect. The intermediate and end products of all pesticidal agents are not known. Many of these may exhibit an acute toxicity which is equal to or greater than the parent compound, as in the case of heptachlor epoxide, produced by the metabolism of heptachlor (68, 88). On the other hand, DDT is metabolized to the nontoxic entity, DDE (45). Metabolic modification of pesticides is not limited to animal and man. Lichtenstein and Schultz (50, 54) contend that plants also convert certain of the insecticides to their corresponding epoxides. Soil conditions, sunlight, air, and rain are also responsible for the decomposition of pesticides into new compounds that are often as toxic as their parents (51-54).

Heptachlor epoxide, dieldrin, and endrin exemplify still another potential danger, carcinogenicity, since they contain an epoxide grouping in their molecule and certain other compounds having the epoxide structure have already been shown to be carcinogens (47). Recent investigations of a number of epoxides indicate however, that only certain species of diepoxides are carcinogenic (83). None of the monoepoxides tested (presumably those compounds more closely related to heptachlor epoxide, dieldrin, and endrin) were found to produce carcinoma in rats. The investigators caution, however, that this work is only preliminary and further study is needed.

Since neither heptachlor epoxide, dieldrin, nor endrin were included in the study, it would be unwise to conclude at this time that these insecticides are not carcinogenic. Recent reviews on insecticides as potential carcinogens have been prepared by Durham and others (17, 21, 59).

Investigators, in their assessment of the biological problems in wildlife, have raised the question of sublethal effects of residual insecticides and have presented some evidence with respect to the subtle activities of such agents. Evaluation of the detrimental effect of pesticides on wildlife has been previously concerned with mortality, or the determination of the numbers and percentages of fish, birds, or mammals that died following the application of a toxicant. However, of equal concern is the morbidity the animals suffer. What effects these toxic agents have on growth, reproduction, mutagenesis, or other biological processes are not fully determined. In chronic toxicity studies with quail and pheasant fed 0.14 mg of certain chlorinated hydrocarbon insecticides daily for 2 months, Dewitt has shown that eggs of reduced hatchability were produced and the resulting chicks were subject to high death rates (15). Additional evidence indicates that pesticide residues do cause genetic changes (7, 12, 73).

#### HOW FOOD IS CONTAMINATED

Food products undoubtedly contain some pesticide residues (77). These contaminants enter the food supply in a number of ways. Crops may be contaminated by direct application, by uptake from the soil and water, or by accidental means such as fall-out or drift from applications to adjacent fields. Lichtenstein, et al. (50, 54) have shown that translocation of pesticides from soil to plants does occur and that certain vegetables tend to concentrate the agents. Evidence also indicates that many of the chlorinated hydrocarbons persist for long periods of time in soil and plant debris (86). Residue concentrations in cereal grains are at times increased by fumigation of storage bins and containers.

Residues in milk and meat may result from direct application to the animal or from the animal's ingestion of residue in feed and water, inhalation of the toxic vapors, and, to some extent, absorption, inhalation, and ingestion from applications to the animal's housing. Waste disposal, runoff from agricultural areas, and direct application of pesticides to water for the control of undesirable aquatic vegetation and marine life often result in the contamination of fish and shellfish (19).

All foods may inadvertently be contaminated during production, in the processing plants, and in the home. Consequently, all food materials provide a

continuous, though extremely limited, source of these potentially hazardous agents.

#### EFFORTS TO SAFEGUARD FOOD

In July 1964, the Federal Committee on Pest Control (FCPC), was established by the Secretaries of USDA, Department of Defense, DI, and DHEW consisting of two members and two alternates from each of the four Departments to coordinate interdepartmental efforts in accordance with the recommendations of the President's Science Advisory Committee in its report "Use of Pesticides" (77). The FCPC provides a continuous review of all direct uses of pesticides by the Federal Government and insures that the Federal programs will be conducted with maximum safety, effectiveness, and economy. Following review, FCPC recommends procedures to achieve the desired results while preventing or minimizing undesirable effects. The Committee recognizes the statutory duties of each Department, and its recommendations are not intended to limit statutory responsibilities. In addition, the Committee's responsibilities extend to pest control programs in which the Federal Government participates through planning, development, supervision, or financing. Furthermore, it coordinates government information, monitoring, and research on pesticides through special subcommittees.

In its initial program of development and evaluation of pest control agents, the USDA realized very early the possibility of harm from residues in food. Consequently, around 1940 this agency began to evaluate the hazards involved (72). USDA studies, including feeding experiments, have contributed valuable information regarding recommended uses, amounts and frequencies of application, and persistence of residues on crops and in meat and milk. Perhaps the most valuable general service provided by this department is the publication annually of recommended uses and the amount and frequency of application of various pest control agents (74).

The USDA is frequently called upon to apply pest control in the field. All of the large eradication and control programs, such as gypsy moth and Japanese beetle, are the responsibility of this department. Quarantine and control designed to reduce the number of pests, and thus decrease chemical pesticide applications, are additional functions. More recently, USDA scientists have been successful in the limited development of alternative pest control procedures, such as radiation sterilization of male insects and the use of sex attractants (73).

The PHS is directly responsible for protecting the public health from hazards of pesticide use. Since 1940, human and animal experiments have been car-

ried out to determine the effect of pesticides on physiological functions (76). In its program the PHS has investigated the uptake, retention, and excretion of chlorinated hydrocarbons, including buildup in body fat; the effect on the organism of residues as shown through short-term feeding trials; and the overall toxicity effect of many pest control agents (30, 71, 77). Methods have been developed to detect toxic residues in air, water, milk, other food, and body tissue. Valuable data have resulted from surveillance of the environment, studies of the exposure of pesticide applicators and workers in chemical plants, and epidemiological investigations of pesticide incidents in homes, factories, and communities (47).

The last and perhaps the most important phase of the work of the PHS is communication. All of the information that can be collected from PHS research and the work of others is made available to state and local health personnel and representatives of universities and industry by means of short courses, consulting services, bulletins, and training in analytical procedures and techniques (79, 81).

Many of the analytical methods used today were developed by the FDA. It has established more than 2,400 separate tolerances for over 125 chemicals and has maintained a constant surveillance of food in interstate commerce to enforce the existing tolerance regulations (76). For example, in 1962 more than 25,000 food samples were analyzed (46). Obviously not all contaminated food can be detected and removed from human consumption, but as the result of the efforts of this agency, the incidence of illegal pesticides in food and the average concentrations of residues in contaminated samples are on the decline (44). Food producers and processors are apparently becoming more conscious of the potential hazards of pesticide residues in food and are making every effort to minimize such contamination.

The DI has the responsibility of protecting the natural outdoor environment from large accumulations of pesticides. Department scientists are seeking to learn more about the effect of pesticides on fish, birds, and other wildlife and to reduce the hazard in this portion of the human food chain. Considerable research is in progress toward the development of alternative pest control agents, both insecticides and herbicides (22).

Not all work concerned with pesticides is being done by the Federal Government; agricultural experiment stations, universities, many state and local health departments, and state departments of agriculture are involved in research, surveillance, training, and regulatory activities. Although much of this work is being supported by Federal funds, the states themselves are spending large sums of their own

money in support of these programs.

This discussion would not be complete without including the contributions of industry. The tremendous amount of developmental work by the pesticide manufacturer is responsible for many of the efficient pesticide agents and must be recognized. It has been estimated that the manufacturer spends an average of 5 years and \$2 million in the development of a single pesticide and reportedly is able to put only 1 of 30 on the market (27). Industry is constantly striving to improve these materials, to perfect relatively safe replacements for the more potentially hazardous agents, and to develop methods of analysis. It spends an estimated 1.7% of sales receipts to investigate potential health hazards of new products before these products are offered to the public (6).

#### ANALYTICAL METHODS

The ultimate control of pesticide residues in food depends upon the development of an efficient surveillance program. The major concern in such a program is the analytical methods used to detect and measure pesticide residues. Analysis of food for pesticide residues is fraught with difficulties. As indicated previously, 60,000 formulations representing more than 900 chemical agents were registered for use as of 1964. These formulations represent all of the chemical species previously listed. Residues must be detected and measured in concentrations of 10 to 0.01 ppm. Food products are of a complex chemical nature, usually difficult to sample, often requiring preservation, and generally difficult to prepare for analysis without loss or destruction of the agent in question. Consequently, the ideal analytical method for an efficient surveillance program would be a rapid screening procedure capable of yielding sensitivity in the area of 0.01 ppm of any of the potential pesticide residues, regardless of chemical species, from a crude extract of the food in question. Obviously such a method does not exist. Methods of analysis available today are long and laborious; are useful for a single pesticide, small groups of pesticides, or a single chemical species; are not completely specific; lack required sensitivity; or require expensive instrumentation and intelligent and well trained operators. Undoubtedly, the time required for analysis is the greatest problem in devising a realistic sampling system and thus an efficient surveillance program. Methods of analysis available consist of chemical colorimetric and titrametric procedures; biological assay methods; gas, paper, and thin-layer chromatography; and combinations of gas chromatography and spectroscopy or electrometric titration (28).

## PREVENTING CONTAMINATION

The utilization of analytic methods on food materials is for the most part an after-the-fact control procedure. While it has been reported that techniques exist for the removal of pesticide contamination from processed food materials (40), investigation has shown that normal procedures followed in the manufacture of milk products are virtually ineffective in removing pesticide residues (48, 49). Consequently, the aim of food producers and processors is to supply food products as low in pesticide residue concentration as possible. A number of publications on the safe handling and use of pesticides are available (76-78, 80, 81, 84). In general, pesticide contamination of food can be minimized by following the recommendations of Federal and state regulatory agencies, observing the manufacturer's instructions on the label, guarding against careless application, and carefully selecting animal feed materials.

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### FIRST ANNUAL REPORT OF CALIFORNIA FOOD PROTECTION AND TOXICOLOGY CENTER

The Food Protection and Toxicology Center at the University of California at Davis, activated on January 1, 1965 has completed its first year of operation and has issued its first annual report, reviewing its accomplishments and outlining its plans for the future. The report describes the objectives and progress of the Center. As a specialized research and training unit, it is concerned with all phases of the environmental science but particularly with the hazards associated with the application of chemicals in producing raw and processed foods, the naturally occurring toxicants and effective agents associated with foods as well as other aspects of food quality.

Several projects involving new areas of research were initiated during the Center's first year of operation. These included a project to determine the relative potency of certain chlorinated hydrocarbon pesticides on the central nervous system; the impact of synthetic organic toxins on soil microorganisms; poultry production and processing practices resulting in the presence of salmonella; and an expanded investigation of certain factors in the hazard of botulism, particularly in prepacked foods.

Other research projects under development include a study of the increasing environmental levels of toxicant residues and possible adverse effects of chronic exposure to humans; use of toxicological agents and the metabolism of these toxicants by microorganisms and animals; the isolation, distribution, and toxicity of natural poisons in food and their

significance in human and animal health; nutritional studies on selected phenolic compounds to improve foods; and a study of the biological and economic implications of pesticide contamination through water drainage.

The Center has the further major objective of producing a greatly increased output of scientists trained in the related disciplines of environmental sciences. Broadly speaking, the Center is concerned with developing new research information, establishing curricula, improving communication within the scientific community, and eventually with improving man's environment.

One of the most important steps taken at the Center during the year to minimize chemical and microbiological hazards to man was the establishment of the Information and Documentation Service. This vital activity will enable the Center to: conduct research on improved techniques for the accumulation and handling of information necessary to the Center's research and training activities; disseminate this scientific information not only to the Center staff but the scientific community at large; develop broad uses for the information by Center-sponsored lectures, seminars and conferences; and to train documentation experts in the environmental sciences. A special working library is being developed and collections being sought include specialized reference works and periodicals, industrial and government publications and reports.