Study Book

For the Training Course:

PESTICIDES and Public Health

Introductory

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FOREWORD

This studybook is made available to students enrolled in the "Pesticides and Public Health: Introductory" course to serve as an aid in seeking an understanding of the conceptual and technological considerations pertaining to pesticides. Such are important in developing and maintaining effective programs in the fields of environmental health and environmental protection. The reader should not be surprised to find the fundamental elements explained in detail for each topic for we have assumed that those attending the introductory course do not have a strong background in the subject based on either study or experience.

For the most part these papers were prepared especially for inclusion in this studybook. However, it should not be considered a citable source. Original research data presented in these papers will be published by the authors in another form in referenced scientific journals. Should you be unable to locate the appropriate reference for these data, we ask that you contact the author directly.

We take this opportunity to express our sincere appreciation to the authors for their participation in this training course and to wish you, the student, rapid progress toward our goal of adequate protection of human health and of the environment.

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PESTICIDES & OTHER CHEMICALS IN THE ENVIRONMENT

Frank S. Lisella

Until a few years ago, the words "environment" and "ecology" were almost exclusively reserved for the scientist's vocabulary. Today they are part of the layman's vocabulary as well. Much of the interest in the environment is due to significant strides in technology which have greatly altered the spectrum of conditions affecting the life and well-being of man. The correlation between technological progress and increased concern for the quality of our environment has two sides. On one hand, advancements in the control of disease and innovations resulting in increased agricultural production have called for the widespread use of numerous chemical agents, causing, on the other hand, concern about the proliferation of the environment with these chemicals and their ultimate impact on the health of man. For example, the past 25 years have been characterized by marked progress in the control of poliomyelitis, tuberculosis, diphtheria, malaria, yellow fever, and numerous other diseases. As early as 1953, it was estimated that at least 5 million lives had been saved and 100 million illnesses prevented through the use of DDT for controlling malaria, typhus, dysentery, and other arthropod diseases (1). The impact upon society of advances such as these has come with mixed blessings, and there has been a definite shift in environmental hazards from those with a microbial etiology to those of a chemical nature. The increased productivity of farmland through the systematic application of pesticides may in turn create problems of a public health nature. Among these problems are the potential threats to the ecosystem, the hazards created by virtue of occupational exposure through the formulation and application of pesticides, and the possible health effects precipitated by chronic exposure to these chemicals.

Thousands of different kinds and combinations of gases, solids, and liquids can, and do, pose potential health hazards to any, or all, segments of the public. It should be pointed out that the home and occupational environments abound with chemicals which are capable of inflicting immediate injury or death. Among these agents are a wide variety of drugs, cleaning, polishing and disinfecting compounds plus an array of substances such as lead-based paints, perfumes, lighter fluid, alcohol, turpentine, gasoline, solvents and thinners, pesticides, and other materials. In fact at any one point in time, there are approximately 250,000 chemical products which are capable of causing human illness, death, or contamination to wildlife and the environment. It has been estimated that approximately 40,000 new potentially poisonous products enter the market each year. In less than 20 years, the use of synthetic chemical pesticides has increased from a level of a few million pounds a year to nearly one billion pounds annually. Today, almost 60,000 different pesticide formulations are now registered in the United States and each of these contains one or more of the approximately 600 different pesticide compounds.

Pesticides have had a tremendous impact on the benefits we have been able to derive from our society. If, for example, we are to look at some of our recorded history, we would find that the literature is replete with writings pertaining to man's continual battle to eliminate or reduce populations of pests.

In the early history of the colony of Virginia, Captain John Smith recorded that in 1609:

> In searching our cashed corn, wee found it halfe rotten and the rest so consumed with the many thousand rats increased from the ships, that we knewe not how to keepe that little we had. This did drive us all to our wits ende; for there was nothing in the country but what nature afforded (2).

Later in 1617, he wrote of rats again;

> . . . they spared not the fruits of the plants, or trees, nor the very plants themselves, but ate them up . . . at last it pleased God, but by what means it is not knowne, to take them away (2).

An arsenical compound, copper acetoarsenite (Paris green) was used as one of man's first pesticides; discovered in 1867, this chemical was first used to control the Colorado potato beetle. Later pesticides played important roles in stemming outbreaks of yellow fever, malaria, typhus, and other vector-borne diseases. While these diseases have been virtually eliminated from the United States, they still remain as threats to the health of people in other areas of the world, and pesticides play a vital role in their control.

In addition to the prevention or elimination of disease, pest control measures are necessary to provide the foodstuffs, fiber and other agricultural items necessitated by our expanding population. The total quantity of food eaten each year by the population in the United States is sufficient to stagger the imagination. The average sized family of 4 people consumes over 2 1/2 tons per year. Meat, poultry, and fish account for nearly one-half a ton, and dairy products close to three-quarters of a ton; fruits and vegetables for well over a half a ton; flour and cereal products, sugar, potatoes, fats and oils, and eggs add up to over four-fifths of a ton. Based on these figures, the U. S. consumer averages more than a ton of food per person per year (3).

The food supply of the country must increase in relation to our expanding population. During 1969, the number of farms in the United States dropped to a new low of 2,971,000. This represented a 54.1% decrease from the 6,500,000 farms 50 years ago (4). Associated with the decline in farms is an obvious shrinking of the total number of acres available for agricultural purposes. Obviously, if the nation's food needs are to be met, the productivity per acre must be increased. Pesticides and other agricultural chemicals play a vital role in this connection. In fact it has been estimated that approximately 70% of the most important agricultural crops produced in the United States cannot be grown successfully without the use of insecticides. Damage by insects lowers the general quality of fruits, grains, and vegetables. Almost all corn and sorghum are planted with organic fungicides for the control of decay. Weed control is necessary and carried out by the systematic application of herbicides. More than 50 different species of insects prey upon stored food and grain products. Insecticides play an important role in keeping damage of these commodities to a minimum. Even with the use of pesticides, the loss of agricultural commodities may exceed $11 billion a year (3).

Thus, we are concerned with the widespread dispersal of pesticides and other chemicals and consequently are placed in a "benefit vs. risk" situation. That is, the advantages to our society must outweigh the detrimental impact the chemicals may have on our environment. In order to ascertain this point, many investigations have been conducted on their presence in the physical environment (air, soil, water) and on their potential harm to humans and wildlife. Each of these points will be considered briefly.

Air

The presence of pesticides in the atmosphere is an important health consideration. Earlier investigations on pesticides in the atmosphere were devoted primarily to drift, and only recently have a sampling device and appropriate analytical techniques been developed. At the present time, ambient air samples are being collected from numerous locations throughout the United States. Levels as high as 486.5 ng/m^3 of ethyl parathion; 162.5 ng/m^3 of methyl parathion; 117 ng/m^3 of p,p'DDT; to as low as 7.6 ng/m^3 of lindane have been detected at certain of the sample sites.

Atmospheric evaluations are also important in maintaining safe working conditions in formulation, manufacturing, and packaging plants. These are important for two basic reasons: first, to determine the actual magnitude of inhalation exposure of workers (both fluctuations in exposure and also integrated exposure throughout the workday); and secondly, to locate contamination sources for purposes of environmental control (6).

The contamination of air by pesticides must be continually investigated in order that we can obtain a clearer understanding between the relationship of these chemicals in the air and human health.

Water

Pesticides may enter water supplies by direct and intentional application; by inadvertent drift into water from adjacent spraying operations; or perhaps, more commonly, by runoff from pesticide treated areas within a watershed (7). During recent years there has been a considerable amount of interest focused on the prevalence of pesticides in surface waters. Our rivers and streams provide water for a large number of quality-dependent users--including those served by municipal water supplies; agricultural and industrial consumers; those desiring propagation of fish and wildlife for aesthetic, commercial, and sport purposes; as well as those used for a variety of recreational activities.

Runoff from agricultural areas is probably the single most widespread and significant source of low level surface water contamination by pesticides (8). The transport of these chemicals from the soil to water may occur while the pesticide is adsorbed on eroded particulate matter, while in solution in runoff water, or by both means.

Pesticide formulation plants, production plants, firms that reclaim used pesticide containers, operations that apply wool preservatives, textile plants that use pesticides for moth proofing and similar industrial concerns are often responsible for the discharge of large amounts of pesticides to a water course. Discharges of this type may frequently be responsible for the mortality of various types of aquatic life within the ecosystem.

The literature contains numerous references to situations where streams have been grossly contaminated by pesticides either as the result of an accident or by sheer carelessness. For example, in Florida a few years ago, a rancher instructed his ranch hand to dispose of 50 four-pound bags of parathion dust (8). The bags were subsequently thrown into a stream which was the water supply for a small municipality downstream. Fortunately, a major disaster was averted because some of the bags were lined with a polyethylene material which prevented the parathion from entering the supply; and the community involved switched to an alternative supply of water. Residues of parathion in the water were still detectable about two weeks after the episode.

In the aquatic environment, we are also concerned with the buildup or biological magnification of pesticides in the flora and fauna. The accumulation of pesticides may occur following the application of the chlorinated hydrocarbons, mercury, and arsenical compounds and other heavy metals. In order for a pesticide to be biomagni-

fied, the compound must be persistent in the physical environment, available to the organism, and persistent once it is assimilated into the biological system (9). Studies indicate that DDT and its metabolites, dieldrin, chlordane, toxaphene, and heptachlor may go through biological magnification in the food chain. Our ultimate concern is with man who may consume the fish, crustaceans, or other components of the food chain and thus contribute toward increasing his body burden of pesticides.

Soil

Pesticides in soils may seriously affect the marketability of crops. Pesticides settling on soil may remain on the surface and later be moved by wind or washed off by rain--or they may penetrate to some depth. Penetration will depend on the characteristics of the pesticides and soil as well as on rainfall and other conditions. A portion of the pesticides in soil may be absorbed by plants or other organisms, and some may be translocated (10).

The accumulation of persistent toxic substances in the ecological cycles of the earth is a problem to which man has to pay increasing attention.

Important factors influencing the persistence of pesticides in soils are the following:

1. Soil type: Pesticides persist longer in soils of high organic content, such as muck soil; however, pesticides are absorbed into crops most readily from sandy soils.

2. Soil moisture: The persistence of some pesticides is affected by soil moisture. Moisture enhances the release of volatile pesticides from soil particles and also influences the breakdown of other pesticides by way of hydrolysis.

3. Soil temperature: The soil temperature has a remarkable effect on the rate of loss of a pesticide. Temperature influences loss through volatilization, as well as breakdown of the pesticide by biological and chemical factors.

4. Cover crops and soil cultivation are also of importance. Soil cultivation increases the disappearance of pesticide residues from soils (11).

Humans

Since 1965, there have been a series of research projects in operation to study the effects of pesticides on human health. These projects are located in 14 different areas of the United States and function through contracts with State health departments or universities. Each of these Community Study projects has three distinct objectives. The first is to determine the types and quantities of pesticides used in the area from season to season and year to year. The second is the determination of the levels of certain organochlorine pesticides in human tissue, and the third is a prospective study of workers occupationally exposed to pesticides. This latter segment of the program may require 10, 15, or 20 years of continued observation to ascertain the possible adverse effects of exposure to pesticides. These studies have yielded much data which serve to increase our understanding of the effects of pesticides on human health. At the Colorado project for example, studies have shown that there is a significant correlation between levels of pesticides in house dust and levels of pesticides in the blood of the members of the family. This suggests that a person's immediate environment may be an important source of pesticides exposure. The Michigan Community Study has been investigating chromosomal aberrations by using cell cultures from peripheral blood. The purpose of these investigations is to compare the frequency of chromosomal aberrations among the exposed group to that of the control group to determine if there are significant differences in the incidence of this condition. Investigators at the Idaho project have noted that tissues collected from the pheasant population in the State contained residues of mercury. This is of signifi-

cance because the wildlife populations may in essence act as "sentinel animals" and may signal human contamination as well. The Arizona Community Study has conducted experiments to define the metabolic pathways of DDT. It is an accepted fact that DDT is metabolized under anaerobic conditions to DDD and under aerobic conditions to DDE. DDD is in turn metabolized to DDA, a water-soluble end product which is excreted in urine. DDE is lipid soluble and is stored in adipose tissue. Recent data suggest that levels of DDE in man may reflect exposure to DDE rather than DDT as is currently accepted. At the Florida Community Study, the interaction between the metabolism of pesticides and drugs has been investigated. It has been shown that certain drugs increase the metabolic breakdown of DDT in man (12).

In addition to the Community Study projects a human monitoring program is in progress, the purpose of which is to determine on a national scale the levels and trends of the more commonly used pesticide chemicals in the general population and in population segments where intensive exposure to pesticides is known or suspected. Samples of adipose tissue are being collected by 100 cooperating pathologists in 40 different States. Primary emphasis is placed upon the detection of chlorinated hydrocarbons and assessing the levels of these compounds, since these compounds are known to concentrate and persist in human and animal fat. The data which have been analyzed to date indicate that blacks have significantly higher concentrations than members of the white population; also, persons living in the South have higher concentrations than those in the North; and males tend to have higher concentrations than females, especially among blacks. This data suggests that several factors influence an individual's concentration of pesticides (12).

Wildlife

Pesticides play an important role in the management of fish and wildlife populations. These chemicals are frequently used for the control of rodents and predatory animals and for the removal of "rough" or "trash" fish from lakes and streams. Many of these chemicals are highly toxic to animals and consequently there have been numerous instances involving situations where animals other than the "target" organism have been harmed. There is also concern over the buildup or biomagnification of pesticides in wildlife species that may be a source of food for man.

Other Chemicals

As with pesticides, we must be concerned with the health hazards associated with both the acute and chronic exposure of persons to other chemical agents. A principal source of concern pertains to the ingestion or the inhalation of chemicals at dosages below the acute toxic levels. The long-term effects of exposure to low levels of compounds that are 1, 2, or 3 orders of magnitude over "background" levels are of particular concern. The problem is complicated by attempting to understand the effects of low-level exposure to combinations of chemical agents.

During the past few years, there has been considerable publicity in both the lay and scientific press with regard to three heavy metals--mercury, lead, and arsenic. Each of these agents creates special problems in our environment and will be discussed separately.

Mercury

The hazards associated with mercurial compounds have been known since ancient times. Inorganic mercurials were used as suicidal agents, abortants, and for therapeutic purposes for many years. Mercurialism as a result of industrial exposure has been a problem of concern for quite some time. The expression "mad as a hatter" exemplified the presence of the illness in the felt hat industry. "Minamata disease" or methylmercury poisoning due to the ingestion of contaminated fish occurred in a village near the Minimata Bay, Japan, from 1953 through the 1960s. The condition affected at

least 121 children and adults of whom 46 died. Attention was again focused on the disease in 1964 and 1965 in Niigata, Japan, when 47 persons became ill, 6 of whom died (13). These episodes, and an incident in Alamogordo, New Mexico, involving a family of 7 in 1969 served to focus attention on the hazards associated with the presence of this agent in the environment.

Mercurial compounds may enter the biosphere from any number of sources. Paper pulp factories which use mercurials to prevent the growth of slime from fungi frequently discharge PMA (phenylmercuric acetate) with their waste water. Paper products which retain mercury and are subsequently combusted might contribute to atmospheric contamination. Industrial concerns which use mercury electrodes in the production of chlorine and caustic soda often release mercury into the air and water. Laboratories where mercury is used in devices for analyzing blood specimens and central supply rooms in hospitals where mercury is frequently used to clean scientific intruments can be a source of concern. The runoff from agricultural areas which have been treated with mercury-based pesticides are a frequent source of contamination to the aquatic environment. Fungi-resistant paints containing mercurial compounds may be a source of contamination to the persons applying them and subsequently to others that may be exposed to the painted surfaces. Mercurials are often used as mold suppressants by commercial laundries, particularly those with diaper services.

The fact that all forms of mercury entering the aquatic environment may be converted to methyl mercury, which is more toxic than other forms, and can be concentrated by fish and other aquatic species is a problem of growing concern. Alkyl mercurials can be introduced into the food chain by the consumption of mercury-treated seeds or meat from animals which have been fed these compounds.

We must be continually aware of the health implications from mercurials and must conduct appropriate procedures to monitor their dissemination in the environment.

Lead

Despite modern scientific advances, lead poisoning or plumbism remains a unique public health problem. The incidence of chronic lead poisoning in children is greater today than in adults, and the fatality and disabling effects are much more marked in children. Occupational poisonings in adults as a result of inhalation of the dust and fumes of inorganic lead are still of concern.

The environment is subjected to contamination by the leaching of lead from geologic formations. It has been estimated that man's activity in the United States alone in 1966 added approximately 700,000 tons of lead to the environment in that year. The contribution of lead from tetraethyl lead in motor vehicle exhausts has been estimated to be 185,250 tons (14). Contamination of the soil and vegetation from air pollution is related to traffic volume. Only a small part of the lead released from vehicle emissions settles and accumulates in the vicinity of the roadways. The majority of the material is transported by air currents and ultimately settles on the soil and vegetation. Lead which has been recovered from surface waters has been attributed to gasoline. This may result in the accumulation of lead in the tissues of fish.

Lead poisoning among children has been the subject of considerable investigation in Philadelphia, Chicago, Baltimore, Cleveland and many other urban areas in the United States. The study in Cleveland confirmed that the susceptible host for lead poisoning is predominantly a pre-school child with a history of pica and that the agent is found in an environment which is easily definable. Continuing investigations of children residing in tenement dwellings, the development of improved analytical techniques and environmental measures are necessary in order to keep lead poisoning cases among the younger population to a minimum.

Arsenic

Throughout history, arsenic has acquired unequalled notoriety as a poison. As early as 2000 B.C., arsenic trioxide is reported to have been obtained from smelting copper and subsequently was used as both a poison and for medicinal purposes (15). The word "arsenic" appears to have been derived from the Greek word "arsenikon" meaning "potent" (16). Copper acetoarsenite (Paris green) was used as one of man's first pesticides; discovered in 1867, this compound was first used to control the Colorado potato beetle.

The use of arsenicals as insecticides is declining in the United States. On the other hand, the use of the arsenical sodium arsenite as a herbicide has increased because of the shortage of certain chemicals (2-4-D and 2-4-5-T in particular) brought about by the Vietnam war. In other parts of the world, the use of arsenicals (as herbicides and insecticides) has apparently not declined or increased significantly in recent years (17). The use of arsenic as a rodenticide has declined in the United States as a result of the advent of the anticoagulant rodenticides.

One publication (18) lists 55 different situations and/or industrial processes within which arsenicals are utilized in one form or another. For example, they are used as decolorizers of glass, pelt preservatives, grasshopper bait, larvicides, amebicides, additives to animal feeds, algicides, and a host of other applications. This same publication points out more than 100 different population groups that may have occupational and/or environmental exposure to arsenic. The list includes airplane pilots, farmers, pest control operators, taxidermists, tannery workers, and many other individuals.

Lead arsenate has been used extensively in the past for the control of insects associated with apple orchards, vineyards, and tobacco crops. It is still used to a limited extent for the control of the Japanese beetle and the boll weevil. Arsenic trioxide is used mainly as a long-term soil sterilant. Sodium arsenite is frequently used as a nonselective spray to control all types of vegetation; however, since this compound has a salty taste, its use in areas frequented by cattle is to be discouraged. Sodium arsenite is also used for aquatic weed control and as a soil sterilant. Disodium methyl sodium arsonate (DSMA) is less toxic to humans and pets and is used for the control of Dallas grass in lawns and turf. Calcium arsenate is used as a preemergence herbicide for the control of crabgrass and chickweed in lawns and turf (19). In recent years the unique herbicidal properties of cacodylic acid and of methyl arsenic acid were discovered. These simple acids, among the first organic compounds known, are highly toxic to plants, but relatively nontoxic to man and animals. The U. S. Forest Service has developed a hatchet that automatically injects cacodylic acid when a blow is rendered to a tree--thus a new application for this material as a silvicide has been created. Arsenic acid is used as a defoliant to facilitate mechanized harvesting of cotton. As postemergence herbicides, the use of simple arsenicals is unsurpassed. They leave token residues and permit germination of the new seed promptly after the undesirable plants have been destroyed (15).

Thus, with this brief background, it can be readily seen that a significant proportion of the population, if not all, is or has been exposed to an arsenical by one means or another.

Man comes in contact with the arsenicals in a variety of ways. The degree of exposure may be related to a person's occupation, the proximity to a copper smelter, the nature of foods consumed, the type of soil in the area, the type of arsenical ingested or applied for medicinal purposes, and a multitude of other factors. For example, shellfish have been shown to contain high amounts of arsenic when harvested from waters containing 0.14 to 1.0 PPM of this chemical (20). Fish are known to concentrate arsenic in their tissues. Residues as high as 40 PPM have been obtained from the oils and tissues of black bass taken from waters in the southern United States. No

arsenic was found in a specialized study of the public water supplies of the 100 largest cities of the United States. The maximum allowable concentration of arsenic for potable waters in various countries ranges from 50 - 150 PPB. The usual daily intake from water in the United States is estimated between 10 and 20 μg. (17). The detection of arsenic in varying amounts in different foodstuffs has led to the establishment of tolerances for this chemical. At the present time, tolerances for arsenic on foodstuffs range from zero in the Soviet Union to 4 PPM for arsenic acid in raw cottonseed meal, 2.6 PPM on most foods, and 50 PPB in water in the United States.

Food products can become contaminated with arsenic in many ways. For example, apples that have been sprayed with lead arsenate for codling moth control can contain as much as 1 to 2 mg. of residue. Wine and cider can contain arsenic, but this is usually removed during processing. Wine yeasts have been shown to contain arsenic in amounts up to 150 - 180 PPM and baker's yeast up to 17 PPM. Meat may contain traces of arsanilic acid that has been used as a growth additive in cattle and poultry feeds. Theoretically, these additives are discontinued several days prior to marketing and in fact, the Food and Drug Administration allows a maximal animal tissue arsenic content of 2.65 μg./g. The arsenicals must be removed from the feed 5 days before slaughter so that the total level of arsenic in edible byproducts is below 1 PPM. At permissible feeding levels of these drugs, the arsenic in muscle rarely exceeds 0.5 PPM even without the 5-day withdrawal period.

Soil concentrations of arsenic can rise to several hundred parts per million after years of spraying with lead arsenate and other pesticides. It has been postulated that arsenic tends to remain in the top layers of the soil thus rendering it sterile to the growth of some plants. Small amounts of arsenic may be translocated by plants grown on heavily contaminated soils. The quantities of arsenic which have been obtained from plants grown under these conditions are not considered detrimental to human health. Potatoes have been shown to contain 1 PPM of arsenic whether they were treated with arsenical pesticides or not (21). While other organic pesticides are gradually replacing arsenical sprays on food crops in the United States, the use of arsenic-containing herbicides and defoliants has increased as indicated earlier.

The arsenic concentration of atmospheric dust has been determined by a number of workers and is reported to be low or absent in most areas. Arsenic has been recovered from the air of areas where coal is burned or smelting operations are in progress. The recommended limit of arsenic in the air is 0.5 mg./m^3. Only minute traces of arsenic have been recovered from the air in the United States. In a survey of 8 English communities in 1952, the arsenic content of air was found to be in the range of 0.037 μg./m^3 (As_2O_3) to 0.075 μg. (18).

Recently, concern has been expressed over the arsenic content of phosphate ores. Phosphates are an essential constituent of many detergents. Thus, many individuals expressed the fact that these compounds may serve to further pollute our aquatic environment. As a result, the soap and detergent industry has directed their research efforts toward finding suitable substitutes for the phosphates.

Conclusions

If we are going to evaluate the impact of these and other chemicals on human health, there a number of avenues we must explore:

1. We must continue conducting long-term prospective epidemiologic studies to determine the significance of low doses of chemical agents on human health. These studies should include investigations of various combinations of chemical agents; e.g., alcohol and carbon monoxide, pesticides and barbiturates.

2. Efforts must be directed toward the development of competency with regard to pesticides and other chemicals by State and local health departments. These

chemicals should receive the same emphasis that is currently being placed on communicable diseases. Concurrent with program development there should be a modification in philosophy, that is, that morbidity and mortality from chemical agents like that from communicable disease is preventable.

3. Morbidity and mortality regulations within individual States need to be strengthened by adding the requirement that illnesses and deaths associated with chemical agents be reported to the agency responsible for the collection of vital statistics. This is imperative if we are to logically assess the hazards associated with the use of chemicals.

4. Research must be continued into non-chemical methods of pest control. Concurrent with this, emphasis must be placed upon improved crop rotation practices, the development of insect resistant crops and similar activities which will eliminate or reduce the need for pesticidal chemicals.

5. We must continue to monitor the presence of chemicals in the diet, in the atmosphere, and in our air, water and soil. Data collected from these monitoring activities must be analyzed to determine their relationship to human health.

On December 2, 1970, President Nixon established the Environmental Protection Agency. This Agency establishes at the Federal level a strong focal point for environmental health activities. In a recent speech, William D. Ruckelshaus, the Administrator of EPA, said:

> "Our goal must be to obtain the capacity to foresee and respond to emerging problems so that the future will not overwhelm us. Environmental problems are hitting us from every conceivable direction. Every time we look at a newspaper we are reminded how ignorant we were yesterday or last year. Asbestos one week, phosphates the next, mercury the week after--and we may be sure others will follow.
>
> "We have been sitting on the sidelines expecting technology to bring us an unmixed blessing of progress and prosperity. We set technology in motion, and expected it to take care of us. In truth, technology was a substitute for thought." (22).

Thus, as is pointed out, it becomes obvious our thinking must change if we are to keep pace with our environmental problems.

Our goal for the future might well be found in the writings of Louis Pasteur who indicated:

> "Two opposing forces seem to be in mortal combat today. One, a force of blood and death--ever devising new means of destruction . . . .
>
> "The other, a force of peace, work, and health, ever evolving new methods of delivering man from the scourges that beset him."

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STRUCTURE-RELATED CHEMICAL CHARACTERISTICS OF PESTICIDES

L. A. Richardson

In the area of chemical properties of pesticides, the only factor more important than chemical structure, is the elemental makeup of the compound. Chemical structure exerts a major influence on the toxicity, reactivity, metabolism and degradation potentials, persistence, and the analytical methodology useful in the elucidating and measuring of most pesticide chemicals. Thus, a basic knowledge of the structural characteristics of pesticides is absolutely essential to all personnel responsible for any area of pesticide use, control, or analysis.

In the short period of time which we have to discuss pesticide chemistry, one can only present an introduction to this fascinating and complex subject. I will provide a brief picture of how these compounds exist in space and how related chemical species differ among the "use groups", insecticides and herbicides. Secondly, I will discuss with you examples of reaction, metabolism, and degradation of "type" compounds.

In order to impress upon you the complexities and importance of pesticide chemistry, please note that there are at the present time some 600 chemical species, from which about 50,000 formulations are available for use. While the problems in pesticide chemistry are not particularly peculiar, the discussion of such a large segment of the chemical industry and the understanding of such a discussion is indeed difficult. In actuality, there are only about 100 chemical species in primary use, about 20 of which we will consider today. Chemical pesticides are produced at about two billion pounds per year at the present time. This is about 10 pounds per capita, or enough poison to kill every human being on the face of the earth. Fortunately, most of these materials are not persistent as the parent compound; and although their decomposition, metabolism and reaction may sometimes produce materials which are even more toxic than the parent, generally speaking, such products are not nearly as toxic as the parent compound and in some cases are virtually innocuous. The structural formulae we will inspect are only for the sake of explanation and discussion; there is no attempt here to coerce you into memorizing them since one of your references has each of them catalogued for you. It would be well for you to note and recall important structural characteristics and elemental differences among the chemical species. As a first principle of segregation, we will consider these compounds, one "use" group at a time, beginning with the insecticides.

Organochlorines are the most prominent of insecticides because they are the oldest, the most used, and because their toxicity is a two-edged sword. They are relatively non-toxic as far as acute symptoms are

concerned, but they are of interest because they are cumulative and may exhibit a more sinister or potential effect. We may also have either a synergistic or an antagonistic activity within the organochlorines themselves or between these materials and other chemical species. In the organochlorines, we have a number of structurally related groups; first of which is the chlorobenzilate or DDT group. The structural relationship depends upon the matrix groups; in this case, we are considering an aliphatic group surrounded by aromatic rings. While virtually each pesticide has both a common and a chemical name, we will consider these materials by their common name; and I will show you how one might arrive at their chemical names. In the chlorobenzilates, we have an aliphatic group as a matrix and the compounds are chemically named on the basis of this aliphatic group. In p,p'-DDT, the matrix is an ethane, thus the final portion of the chemical name of this compound would be ethane. On the number one carbon of the ethane group, one finds three chlorines. Two phenyl groups are attached to the number 2 carbon and in the para-position of these phenyl groups we find a chlorine. Consequently, the chemical name for this compound would be 1,1,1-trichloro-2, bis-para-chlorophenyl ethane. The bis simply indicates that there are two phenyl groups tied to the number two carbon.

If we look at o,p'-DDT, we find once again that the basic structure, the matrix, is an ethane and again we have two phenyl groups tied to the number two carbon. Once again, we also find that each of the phenyl groups has a chlorine. In this case, however, the chlorine atom of the first phenyl group is in the ortho position. In the second phenyl group, or the prime phenyl group, the chlorine is in the para position as we found in p,p'-DDT. O,p'-DDT, then, is an isomer of p,p'-DDT, a positional isomer. Isomerism changes the characteristic of compounds. In this case, p,p'-DDT is somewhat more toxic than is o,p'-DDT. We also find that we can separate these materials on a gas chromatographic column. Methoxychlor has the same basic or matrix group, but the groups associated with the aromatic rings are methoxy rather than chlorine. We have, of course, changed the toxicity and the characteristics of the compound. Methoxychlor and p,p'-DDT are quite different from the standpoint of toxicity and certain other characteristics. TDE or DDD is another member of this group. In this case, we have only two chlorines on the number one position of the basic matrix while the reactive groups on the aromatic rings are exactly the same as in DDT. The relationship between perthane and TDE is very similar to the relationship between methoxychlor and DDT. The two chlorines on the aromatic ring of TDE have been replaced by ethyl groups. Once again, the characteristics of this compound has changed. Kelthane is quite similar to p,p'-DDT except that kelthane has a hydroxyl group on the number two carbon whereas DDT has a hydrogen. The characteristics of this compound are obviously different from those of DDT and, as a matter of fact, the chemical name of the matrix group is different. This compound actually has ethanol rather than ethane as its matrix. If we consider the matrix group to be ethanol, we must change the order of numbering the carbons in the molecule. Thus, Kelthane is chemically called 1,1-bis parachlorophenol 2,2,2, trichloroethanol.

The second principal group of organochlorine insecticides is the cyclodiene, or as is sometimes referred to as the aldrin type. These compounds are named on the basis of the cyclodiene group. The three compounds shown in this first group have napthalene as the matrix. Aldrin readily reacts to form the compound dieldrin. If you will notice, there is a position on the aldrin molecule on which we can institute a minor change and obtain the structure just below, dieldrin. The simple change between these two molecules is a result of oxidation, or as it is usually referred to, epoxidation. The double bond between the 6 and 7 position of aldrin, which is occupied by hydrogens, has been broken with the addition of an oxygen bridge. Dieldrin is the form in which you normally find the residue of aldrin applications. A compound similar to aldrin which is referred to as isodrin, and to the best of my knowledge is not used as a pesticide, also epoxidizes to the third structure endrin. Aldrin and isodrin are isomers. Similarly, dieldrin and endrin are isomers. These stereoisomers differ in their structure only in that, if we would assume that the solid lines in the chair configurations are in the plane of the screen, the epoxide group in dieldrin would point back into the screen whereas the epoxide group in endrin would point out toward the audience. Once again the properties of the two isomers are somewhat different. Endrin is considerably more toxic than dieldrin. Dieldrin has a greater tendency to concentrate in human tissue, thus I suppose we could say it is more soluble in fatty material. Finally, these two isomers are easily separated on a chromatographic column.

The second subdivision of the cyclodiene, or aldrin group, consists of the indene molecules of chlordane, heptachlor, and heptachlor epoxide. Since the matrix of these compounds is the indene ring, they are named chemically as substitutedly indenes. Chlordane is the oldest of this group and unfortunately is still being used to a considerable extent although its usage has decreased in favor of other insecticide agents; one of them being heptachlor. I say "unfortunately" for two reasons; first, it is the most persistent chlorinated insecticide, and second, it is extremely difficult to analyze by gas chromatography because chlordane consists of a number of isomers and these isomers are separated into a multitude of peaks on the gas chromatograph column. Separate isomers show separate peaks on the chromatogram when using gas chromatography and also give separate spots to some extent (usually a streak) on thin-layer chromatograms. Consequently, they have a tendency to mask other insecticides which might be present. Heptachlor is very similar to chlordane and is a popular insecticide although somewhat less popular than it was a few years ago. Heptachlor is never found in human or animal tissues and is found in a rather reduced quantity in any residue determination if one considers the amount applied. The reason for this is that heptachlor readily oxidizes to heptachlor epoxide. This epoxidation is identical to that of the epoxidation of aldrin to dieldrin in that a double bond is fractured and replaced by an oxygen bridge. The resulting product is toxicologically opposed to that of the DDT-DDE conversion. DDE is essentially non-toxic. Heptachlor epoxide, however, is just as toxic if not more so than the parent compound, heptachlor.

The third group of chlorinated insecticides consists essentially of a single compound or, at any rate, a single compound represented by a number of isomers; the hexachlorocyclohexane series commonly referred to as benzene hexachloride or BHC. The compound pictured is lindane, the gamma isomer, and the only isomer that is insecticidely active. These are cis-trans isomers and one can readily picture the various transpositions of chlorine and hydrogen in the structure which produce the different isomers. As I indicated, gamma BHC (or HCH as it is sometimes correctly named), or lindane, is the only insecticidely active isomer; however, the beta isomer is a good indicator of BHC contamination because it is the most persistent.

The fourth and final group of chlorinated insecticides consists of the fumigate group. Fumigants are aliphatic compounds and, of course, carry aliphatic names. Methyl bromide, ethylene dibromide, and methylene dichloride are the most popular fumigants. Methyl bromide is a potentially dangerous material whose formulations have been utilized as seed treatments and for the protection of residue problems in that hydroxyl, sulfhydryl, and amino groups are metholated, and hydrobromic acid is released. Thus, we have an inorganic bromine residue in the product. This pesticide also presents a hazard to the applicator. The second principal group of insecticides consists of the organophosphates. We will talk about four groups of these compounds and point out the differences in structure. From the chemical standpoint, organophosphates are esters of phosphoric acid and are readily formed from, and degraded to, substituted phosphoric acid and alcohols.

Two types of bonding are important from the standpoint of organophosphate characteristics and properties. The first, is involved with the association between phosphorus and an isolated oxygen or sulfur. From the standpoint of valence, this association is a double bond. With respect to properties, it is a coordinate covalent bond; that is, the phosphorus provides the electrons for the union rather than a sharing of electrons as with the simple double bond or covalent bond. Such relationship results in a more positive phosphorus. When this isolated atom is oxygen, a more electronegative element, the phosphorus becomes extremely positive and the compound becomes even more polar, more water soluble, and more toxic.

The second bonding feature of interest deals with all the elements directly attached to the phosphorus. For the most part phosphorus is bonded to carbons only through oxygen or sulfur, however, a few compounds have direct phosphorus carbon bonds. Since the carbon-phosphorus bond is much more easily broken, such compounds are more readily degraded or converted.

I have previously stated that all organophosphate insecticides are esters of phosphoric acid. Normally these compounds are named as esters, however, complexity often causes the naming system to break down and we frequently find incorrect chemical names applied. Perhaps we should consider some of the problems in naming and some of the hints, as to structure, which we can gather from the chemical name. All phosphates

contain various groups whose names are preceeded by a capital S, O, or N. When such is observed in the name, it simply means that such groups are tied to the phosphorus through a sulfur (S), or oxygen (O), or that such group is attached to a nitrogen (N). The second major rule and hint deals with sulfur, since sulfur is contained in almost all organophosphate insecticides. Where a sulfur is in the coordinated, or isolated, position with phosphorus, the compound resembles a ketone and is referred to as a thiono phosphate or phosphorothionate. If the sulfur is in the side chain linkage, the compound resembles a thio alcohol and is referred to as thiolo phosphate or a phosphothiolate. Finally, those compounds having a direct carbon-phosphorus bond are called phosphonates and those having no direct carbon-phosphorus bonds are referred to as true phosphates.

Organophosphate insecticides may be considered in each of four groups. The first, alkene group is represented by bidrin, dichlorvos, and trichlorofon. Bidrin and dichlorvos are phosphates. Trichlorofon is an example of a phosphonate. Trichlorofon fits the category as a "similar to" the vinyl group. The manufacturer removed the typical vinyl grouping by saturating the carbons with a hydroxyl and a third chlorine. None the less, trichlorofon is characteristically a vinyl type structure. A second interesting characteristic of this compound is that it is hydrolized to chloralhydrate, commonly referred to as "knock-out" drops.

The second group of organophosphate insecticides is the aliphatic or alkane type. The compound dimethoate is a good example of this group. Pay particularly close attention to the side chain group attached through the second sulfur atom. The particular group of interest here is the CONH group, referred to as a carbamoyl, also referred to, at times, as a peptide linkage which you probably recall from amino acid groups as they combine to form proteins. This carbamoyl group is characteristically similar to a carbonyl, except that it results from carbamic acid rather than carbonic acid. So, we have in this compound a little of what we are discussing now and a bit of what we will be discussing later, the carbamates. This is also an example of a phosphorodithioate, since we have two sulfurs in the molecule. Dimethoate, often called cygon, is not terribly toxic and none of the parent compound remains as a residue. It is readily decomposed by hydrolysis. The second compound, malathion, has experienced a tremendous increase in use in the last few years. We have been told that it is not particularly toxic but have had some difficulties with it. I suspect these were concerned with large concentrations. Malathion does oxidize to malaoxon; that is, the sulfur indicated by the arrow bond to phosphorus, is replaced by oxygen. Malaoxon is more toxic than malathion. The fact that malathion is generally considered to be rather nontoxic indicates that the positive phosphorus is in some way modulated. The diester grouping of the side chain is interesting and may have something to do with the reduced toxicity of this molecule. The third compound in this series is phorate or thimet. This compound contains two rather interesting points; one, the name. We might have a tendency to look at it with three sulfurs and to name it as a phosphorotrithioate. Actually, we consider the thioethyl group on the end of the side

chain, and name the compound as a dithioate. The second interesting point also deals with that third sulfur which can be oxidized to a sulfoxide, that is one oxygen attached, or a sulfone, two oxygens. The oxidation to a sulfoxide renders this compound considerably more toxic than the parent. This is also true of any compound so constructed that a sulfur can be oxidized to a sulfoxide or a sulfone. This oxidation can take place on any sulfur which is not attached directly to the phosphorus.

The third type of organophosphorus insecticide consists of the aryl, or aromatic types. In essence, these compounds are acid anhydrides of phosphoric acid and phenols. Some of the phenols perhaps may be a bit difficult to recognize since they are also substituted. In the reaction of phosphoric acid and phenol, water is split out, forming an acid anhydride. Acid anhydrides are notoriously easily hydrolized; and as they are hydrolized, they are once again returned to phosphoric acid, howbeit substituted, and phenols, the alcoholic moiety. This phenol, or alcohol, is generally also substituted.

Parathion is an extremely toxic compound and is readily converted to paraoxon, which is, of course, more toxic than the parent. As the oxygen analog, the phosphorus again becomes more positive, more soluble, and more reactive. This is probably the reason for the increased toxicity. Parathion, as you know, is readily decomposed and metabolized.

The compound methyl parathion has a slight structural modification from parathion, methyl groups on the ring instead of ethyl. The reactions, utilization, and toxicity of this compound are quite similar to parathion.

Ronnel is a chlorinated phenolic phosphate, useful in qualitative analysis. Having chlorine, sulfur, and phosphorus moieties, we can use diverse analytical methods and readily establish positive identification. Guthion is a rather toxic compound which contains a diazo structure in the aromatic side chain. Actually, it is referred to as a triazo structure and is named as a benzotriazine. The last compound that we will look at in this group is EPN. The letters EPN stand for O-ethyl-O-paranitrophenyl phenyl-phosphonothioate. The name indicates, and you will recognize from the structure, that this is again a phosphonate. That is, the phenyl group on the left is tied directly to the phosphorus, and the bond is between the phosphorus and the carbon. EPN, as parathion, and methyl parathion, is hydrolized to paranitro phenol

The fourth and final group in the organophosphate insecticides consists of TEPP. Tetraethyl pyrophosphate is a rather innocent looking compound, but as I am sure you all know, is an extremely toxic one. I doubt that tetraethyl pyrophosphate has any appreciable hazard except to the applicator and to anyone accidentally exposed. TEPP unfortunately is being used even today but in rather small quantities, fortunately for the most part, by rather well oriented pest control operators.

Carbamates are the third group of insecticides of particular importance at the present time. Carbamates are named as esters of carbamic acids and their structures contain the carbamate stem OCONH. Carbamates are reported to have low mammalian toxicity, but there are some instances where they can be, and have been, made extremely toxic by reaction. Carbamates are surface sensitizing; there have been cases of dermatitis resulting from the use of carbamate insecticides. They produce some questionably hazardous decomposition products and, certainly at this point in time, need a considerable amount of investigation. Carbamates are utilized as insecticides, herbicides, and fungicides. This doesn't mean to imply that the same compound can do all three jobs, but there are members within this chemical species which can do one or the other, and in some instances, more than one. I've classified the carbamates as monomethyl, or n-methyl, and dimethyl, or n,n-dimethyl. N-methyl or n,n-dimethyl refers to the substitution of the nitrogen on the carbamate matrix. As we look at some of the structures, I can point out much more easily just what I am referring to. The monomethyl compounds are the most labile; they are usually solids, probably due to the hydrogen bonding on the NH group. We will discuss the reactions more completely later.

The first compound which we look at, sevin, one of the monomethyls, is said to be a reasonably safe material. There is considerable investigation currently in progress on the metabolism of this agent. As I indicated, these are esters of carbamic acid; that is, carbamic acid and an alcohol. The compound sevin contains a rather complex alcohol, naphthol.

The second compound of interest is the one referred to as temik. Temik is basically an oxime. The carbamate moiety on the right is mono-substituted by a methyl group, thus a monomethyl carbamate. On the left of this structure you will notice that once again we have a sulfur positioned between two carbon atoms. This sulfur oxidizes rather readily to a sulfoxide, that is the addition of one oxygen, and eventually to a sulfone, the addition of two oxygens. As the sulfoxide the compound temik, which is referred to as temik sulfoxide, is extremely toxic. The sulfone, that is, temik sulfone, is not quite as toxic but still more so than the parent compound. While the parent compound may not be particularly toxic, it is readily and easily converted to a toxic compound.

The second group of carbamates, the dimethyl, are much more stable to heat and light and are usually liquid. Both their stability and the fact that they are liquid appear to be associated with the lack of hydrogen bonding. The lack of hydrogen bonding reduces the rigidity of the compound with the resulting liquid state. In addition, methyl saturation (not easily hydrolyzed) of the nitrogen enhances stability. The compound dimetilan is an example of this group. The carbamate matrix is on the right; however, it doesn't look greatly different from the left side, which is referred to as a carbamoyl.

The second use group of pesticides which we will consider is herbicides. Herbicides, as I indicated to you in the beginning, are not well understood, at the present time. Their potential, the toxicity of the parent compound in many cases, and the decomposition products, and metabolites of many of the herbicides need to be studied extensively. We have experienced a great deal of controversy and hopefully some interest over the use of herbicides in Southeast Asia. There are those who are concerned about their long-term effect on the ecosystem.

There are certain chemical species of herbicides which may be potentially dangerous, and in this discussion we will endeavor to indicate those which could produce potentially hazardous decomposition products. The first herbicide compound we will consider is CIPC, chloroisopropylcarbamate. Looking at the substituted groups on the amino of the carbamate matrix, we notice a mono substitution; however, it is not a mono methyl as we found in the insecticides. In this case it is a mono substitution by an aromatic component; a chlorinated phenol. The reactions on this compound are similar to those of insecticidal carbamates, with the exception that hydrolysis, in this case, has been shown to yield analine, at least in soil.

The second compound, ordram, is a thiocarbamate which we can consider to have a seven member ring. We can visualize this compound as disubstituted carbamate nitrogen. The carbamate matrix includes one oxygen and one sulfur rather than the two oxygen atoms with which we are familiar. Ordram to some extent is similar to temik in that the sulfur can be oxidized to a sulfoxide or sulfone and as such will be considerably more toxic.

A third species of herbicides is the substitutes ureas. Monuron is an example of a urea herbicide and is a reasonably popular agent. I'd like to call your attention to the urea stem in this case and to make sure that you are able to differentiate between the urea and the carbamate matrices. You recall that the carbamate matrix results from carbamic acid which is NHCOOH. Consequently, the carbamate stem is a substituted NH_2COO. Urea, on the other hand, is NH_2CONH_2, and here it is substituted by a ring structure on the left which looks very similar to the compound CIPC. However, on the right side we have lost the acid radical and returned to a substituted NH_2 as we would find in urea. These compounds are named as mono or dimethyl urea with the substituted products preceding that name. Thus, for monuron we have 3,4, chlorophenyl-1,1 dimethyl urea.

The fourth group of herbicides consist of the metallo-organics. Methane arsonic acid is probably the best known, or was the best known until recently, of the metallo-organics. It is usually applied as a sodium salt and is a rather simple straight chain material. Cacodylic acid, perhaps because of the furor over Viet Nam, is now the best known of the metallo-organic herbicides. The chemical name of this material is dimethyl arsenic acid. The toxicity of this material is in the area of about a gram per kilogram.

The fifth group of herbicides consists of the inorganics, such as arsenic trioxide and arsenic pentoxide. Arsenic pentoxide in particular is very toxic and has a tendency to persist for a long period of time in the soil. These compounds are comparatively simple straight chain inorganics.

The sixth and seventh group of herbicides consists of the triazoles and the triazines. Amino triazole, amitrole, is a very reactive material and has been known to be goitrogenic in animals on continued feeding of relatively high concentrations. This is the one that was involved in the famous cranberry affair which some people have indicated was only political. None the less, it is not particularly difficult to appreciate the concern, be it true or sham, because of the triazo ring. Additional information that it is carcinogenic in large concentration is perhaps some defense of the cranberry incident. Simazine is an example of a symmetrical triazine. The azo ring structure does indicate some cause for concern with this particular material; however, the compound, as appears to be true of all symmetrical triazines, is very stable.

Dinitro-orthocresol (DNOC) is an example of phenolic herbicides, and while it may be a bit extreme, I believe it presents a potential problem with phenolic compounds. DNOC is, of course, a very toxic material and it is carcinogenic. It is an excellent weed control agent but is being replaced by herbicides which are probably just as effective and not quite as hazardous. An interesting point on DNOC is that a number of years ago it was being prescribed as a weight control agent.

The ninth group of herbicides, the aniline compounds, can be represented by trifluralin. It is an interesting compound because it is one of the few fluorine pesticides in use. While I have considerable concern about analine compounds, this particular one seems to be of little concern since it is relatively nontoxic and appears to be relatively stable. Actually, only one propyl group from the nitrogen is lost and the resulting product has a very low toxicity. The second compound in this group is the one referred to as stam. Another name for it is propanyl, or 3,4,dichloro propionanilide. This compound readily hydrolyzes to dichloro analin and is a compound worth worrying about. More recently it has been shown that the analine compound in the presence of certain soil micro-organisms is further degraded to a diazo compound, also worth worrying about.

The tenth group, the amides, is represented here by diphenamid. It is a dimethyl diphenyl acetamide. The compound is relatively nontoxic and is apparently removed from the body as a conjugate found in urine. Apparently, the conjugation takes place through the nitrogen with glucose or possible other sugars. The amide group, of course, is the $CONH_2$; the hydrogens on the nitrogen having been replaced by two methyl groups. Differentiate this group from the urea compounds which are NH_2CONH_2 with substitutions on the nitrogen; and from the carbamates which are $OOCNH_2$ with substitutions on the nitrogen.

The eleventh and final group of the herbicides which we will consider is the organic acids. These are very persistent compounds howbeit they are relatively nontoxic. Relative toxicity, of course, is sometimes a bit difficult to visualize. Perhaps one of the best known of the organic acid herbicides is 2,4-D, and contrary to what we sometimes hear, 2,4-D is more toxic than DDT. Benzoic acid is not a particularly good herbicide, but it is a good model since it is reacted with chlorine, methyl groups, and amines, to produce effective herbicides. Benzoic acid itself is relatively nontoxic; it is about as toxic as table salt. Dacthal is a good example of the modification of benzoic acid to produce a useful and relatively safe herbicide. It is substituted with both chlorine and methyl groups. The herbicide dalapon is an example of a straight chain or aliphatic organic acid.

In this brief period of time we have emphasized the matrix and reactive groups of type compounds of the most prominent pesticides. A limited number of reactions have been discussed as well as some of the handles available for analysis. It is my hope that you will appreciate the diverse nature of pesticide chemistry, that you will be able to distinguish between the various chemical species involved and that we will all continue to take steps to minimize the potential hazards of chemical pesticides.

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INTRODUCTION TO PRINCIPLES OF TOXICOLOGY

Thomas B. Gaines

1. Definition: Toxicology is a science that deals with the action of poisonous materials on living cells and tissues, the response of the living structures, and the detection and identification and evaluation of safety of these poisonous materials.

2. Divisions of Toxicology, by Loomis:

Environmental	Economic	Forensic
Pollution	Development of Drugs	Diagnosis
Residues	Food additives	Therapy
Industrial Hygiene	Pesticides	Medicolegal Aspects

3. Scientific Disciplines involved: Chemistry, biochemistry, pathology, biology, pharmacology, physiology, biometrics.

4. Types of injury resulting from poisons:

   A. Gross injury:
      1) Death
      2) Sublethal symptoms - dizziness, respiratory difficulty, vomiting, tremor, convulsions, etc.
      3) Retardation of development
      4) Photo sensitization, skin irritation

   B. Pathology:
      1) Organ weight change
      2) Microscopic changes in histology
         a) Light microscopy
         b) Electron microscopy

   C. Hematological changes (WBC, hemoglobin, hematocrit, differential) and changes in clinical chemistry.

   D. Neurotoxicity - development of paralysis (triorthocresyl phosphate).

   E. **Teratogenesis** - effect on fetal development:
      1) Thalidomide incident
      2) chlorinated dibenzo-p-dioxins, impurities in some compounds

   F. Carcinogenesis - development of malignant tumors:
      1) Very controversial with regard to pesticides

G. Hypersensitivity

H. Induction or inhibition of enzyme activity such as microsomal enzymes of liver.

I. Mutagenesis - genetic change

J. Changes in behavior

5. Factors influencing degree of toxicity:

Compound	Sex
Dosage or exposure levels	Age
Duration of exposure	Interaction of compounds
Route of exposure	Nutrition
Species and strain differences	Disease
Temperature and other environmental factors	

6. Toxicant must reach "site of action" to result in injury. This occurs by way of the circulatory system after the chemical is absorbed into the system from the gastrointestinal tract, lung, or percutaneous route. En route to the "site of action" the toxicant may be bound to proteins and altered or removed, may be excreted by the kidneys or by the respiratory tract or sweat glands, or the molecule may be altered by certain enzymatic systems in various organs, or may be deposited in storage tissues.

7. Factors affecting absorption:

1) Oral route
   a) Compound
   b) Type of solvent
   c) Dilution of the dose
   d) Fasting state of the animal

2) Dermal route
   a) Compound
   b) Solvent or physical state of material
   c) Size of area of exposure
   d) Condition of exposed skin

3) Respiratory route
   a) Physical state of material
   b) Efficiency of absorption in order of sprays, dusts, gases
   c) Particle size - particles in excess of 20μ in diameter are seldom inhaled. The upper respiratory tract tends to capture particles between 5 and 10μ size. The alveoli are most efficient in capturing particles of 0.1 to 3.0μ in size.

8. Selective toxicity - The injury of one kind of living matter without harming some other kind with which the first is in intimate contact. The living matter to be injured may be referred to as the <u>uneconomic species</u>, and the matter which is to be unaltered as the <u>economic species</u>.

9. Measurement of toxicity:

   A. 1-dose ED_{50} or LD_{50}: calculated dose to produce some specific effect or death of 50% of test animals.

   B. 90-dose ED_{50} or LD_{50}

   C. Chronicity factor: 1-dose LD_{50} (mg/kg) ÷ 90-dose LD_{50} (mg/kg/day)

   D. Subacute index

   E. ET_{50} and LT_{50}: time required to effect or kill 50% of test animals.

   F. EC_{50} and LC_{50}: concentration required to effect or kill 50% of test animals.

   G. Response to graded dosage levels.

   H. No significant effect level: dosage level at which no effect is observed in experimental animals. In reality it may be an indication of our lack of ability to detect an effect. Any amount of chemical that is taken into the body probably produces some effect.

10. Tests in Laboratory Animals:

   A. Route of exposure:
      1) Oral
      2) Percutaneous
      3) Inhalation
      4) Parenteral by injection

   B. Duration of exposure:
      1) Acute toxicity - single dose, range of dosage levels given to arrive at LD_{50} value, lowest lethal dose, and lowest dose producing signs of poisoning.

      2) Subacute toxicity - generally considered 90-day test and if by oral route chemical is usually given as a component of the diet.

      3) Chronic toxicity - 2 years in rats and mice, possibly longer exposure in dogs and primates.

   C. Tests to detect teratogenesis and effect on reproduction:
      1) Teratogenesis - pregnant female dosed during organogenesis to determine effect on fetus.

      2) Reproduction - animal usually fed chemical in diet at graded levels and studied through 3 generations.

   D. Potentiation - effect of combination of 2 chemicals in which the effect is greater than additive, for example: 1/4 LD_{50} of one compound plus 1/4 LD_{50} dose of other compound = 1 LD_{50}.

   E. Sensitization: injection followed by delay. Then challenge injection given resulting in substatnially greater reaction than after original injection.

   F. Eye irritation: chemical instilled in eye and observations made on effect on conjunctive (swelling), cornea (ulceration or opacity), and iris (inflammation).

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METABOLISM, STORAGE AND EXCRETION OF TOXICANTS

M. F. Cranmer

UPTAKE

1. Modes of Administration: Oral
   Subcutaneous
   Intramuscular
   Intravenous
   Inhalation
   Percutaneous

2. Rationale for Different Modes of Administration
   Ease
   Speed of Action
   Amount taken up by tissue where drug is active

3. Modes of Drug Preparation:

   Encapsulated solids for oral administration
   Solutions for parenteral administration
   Extra ingredients added, e.g., thiopental plus bicarbonate to increase solubility
   Sustained release preparations

4. Gastric and Intestinal Uptake:

   Factors determining uptake:
   High for: low degree of ionization
   high lipid/water partition coefficient
   small molecular size, if molecule is water soluble
   Some agents taken up by special membrane mechanisms, e.g., Na^+, sugars, amino acids, 5-fluorouracil

5. Degree of Ionization Determined by Henderson-Hasselbach equation:

$$pH = pK_a + \log \frac{\text{base form}}{\text{acid form}}$$

Acid: $\underset{\text{acid form}}{HA} \rightleftharpoons H^+ + \underset{\text{base form}}{A'}$ thus ionized form is base form A'

Base: $HB^+ \rightleftharpoons H^+ + \underset{\text{base form}}{B}$ ionized form is acid form HB^+

Examples: acids aspirin, barbiturates
bases caffeine, quinine, procaine

Most drugs are unable to cross mucosa when they are ionized; hence:

a) Rate of drug uptake determined by concentration of drug in unionized form.

b) Equilibrium drug distribution between stomach and blood is such that the concentrations of unionized drug are the same on both sides of the membrane but ratio R of Drug between plasma and stomach = $\frac{\text{acid form}_p + \text{base form}_p}{\text{acid form}_o + \text{base form}_o}$

Where p is plasma and o is stomach or intestine

Large difference between stomach pH and plasma pH assists uptake of acids and hinders uptake of bases. Uptake of acids from stomach known as ion trapping.

Rate of drug uptake and equilibrium drug distribution affected by alkalinization of stomach with bicarbonate; this decreases acid uptake and assists uptake of bases.

Drugs which are almost insoluble in water may be taken up sporadically and haphazardly from the stomach since they do not dissolve in the lumen; e.g., glutethimide.

6. Inhalation

Gases inhaled and diffused across alveolar membranes; e.g., gaseous general anesthetics.

High lipid solubility, small molecular size and high alveolar permeability result in almost instantaneous equilibrium of general anesthetics with blood.

Aerosols are important route of entry of toxic substances; polluted air, cigarette and marijuana smoke.

References: 1. Drill, Ch. 3, pp. 21-33
2. Goldstein, pp. 106-129

DISTRIBUTION AND SPECIFICITY

1. Body Compartments

Total Body Water	60%
Extracellular Water	17%
Circulatory Plasma Water	4%
Whole Blood Volume	8%

2. Apparent Volume of Distribution

The region of access of a drug may be determined from the drug concentration C in plasma water and the amount of drug administered X.

Apparent volume of distribution $V_d = X/C$

From V_d it is possible to predict which water regions the drug has access to.

Only valid for drugs which do not partition into lipid or plasma protein and for drugs that are not rapidly metabolized or excreted.

Sucrose, mannitol, distribute in extracellular space.

Alcohol distributes in total body water.

3. Binding: Blood contains erythrocytes and plasma protein, both of which may bind drugs.

Erythrocyte membrane may absorb gaseous and volatile anesthetics.

Binding (Cont.)

Plasma protein binds a great variety of agents.

Proteins are:
1. γ globulin
2. α and β lipoproteins
3. albumin

α and β lipoproteins bind cholesterol, steroid hormones. Albumin by far the most important drug binding protein; Constitutes 50% of plasma protein.

Albumin has specific sites for binding anionic, cationic and neutral molecules. Sites are lipid soluble pockets in protein; pockets also contain charges which attract opposite charges of drug molecule.

Binding can be saturated, i.e., limited number of molecules may bind albumin even at high drug concentration.

If drug binds with high affinity to albumin, this may affect drug distribution, rate of drug uptake into organs, metabolism and elimination.

Drug interactions occur through competitive binding of two drugs to albumin, e.g. ethylsulfadiazine + tolbutamide.

4. Distribution

Determined by:

1. Concentration of drug in blood.
2. Rate of transport across blood-tissue barrier (through capillaries).
3. Rate of blood perfusion of organ.
   Time for passage of blood volume through organs:

Brain	30"
Visceral organs	30"
Muscle	15'
Fat	3 hrs.

5. Transport

Determined by:

1. Lipid solubility.
2. Extent of ionization.
3. Molecular size, if drug is water soluble.
4. Polysaccharides and proteins also able to pass out of capillaries by unknown transport mechanisms.
5. Blood brain barrier relatively impermeable to water soluble and large molecular weight compounds.

6. Kinetics

A. Zero order absorption or elimination; when drug is absorbed or eliminated at a constant rate regardless of concentration, e.g. alcohol oxidation.

B. First order absorption or elimination; when drug is absorbed or eliminated at a rate which is proportional to concentration. Most elimination is first order.

Half-life - time taken for drug concentration to drop to half its original level.

$\ln \frac{c}{co} = -kt$ where c = concentration
co = original concentration
k = rate constant
t = time

Half-life $t_{1/2}$ related to k $t_{1/2} = \frac{0.7}{k}$

7. Dosage Regimens

If drug activity is exerted rapidly and ceases rapidly after cessation of administration, constant infusion may be necessary, e.g. nitroprusside in hypertensive patients.

If drug activity is exerted slowly and drops slowly after cessation of administration, then concentration of drug builds up slowly towards plateau value. Drug may be given at fixed intervals. However, if drug action is required rapidly, then a high loading dose is given initially to cause rapid buildup of drug, followed by smaller maintenance doses thereafter, e.g. chloraquine administration in treatment of malaria.

8. Factors Affecting Drug Selectivity

1. Selective site of administration, e.g. local anesthetics; drugs administered topically.
2. Selective distribution of drug.
3. Selective pH of drug activity.
4. Selectivity of receptor site or receptor enzyme of drug, e.g., specific action of penicillin on bacterial all wall synthesis accounts for efficacy and lack of toxicity of antibiotic.

REFERENCES

1. Drill, pp. 25-30

2. Goldstein, pp. 130-194

PESTICIDES OF PUBLIC HEALTH SIGNIFICANCE

Harold George Scott

Tens of thousands of chemicals have been evaluated for insect-, rodent-, weed-, and fungus-control. Hundreds of these are in daily use in the pest control field, and additional materials are being developed continually. As a result, even individuals engaged in pesticide research find it difficult to stay abreast of this vast and rapidly changing field.

Two aspects of pesticide hazard need always be considered: (1) The toxic hazard of the material to man and (2) the total environmental effect of the pesticide. Decisions regarding use should always be based upon adequate consideration of both of these hazard aspects as well as upon effectiveness of the substance.

Essential to comprehension of pesticides is an organized knowledge so unfamiliar chemicals can be associated with known materials and present background of knowledge can be used as a basis for understanding the new chemicals. As advances are made in pesticide knowledge, greater understanding of their toxicity to mammals is obtained. It should be emphasized, that degree of toxicity cannot be determined by the relative position of the pesticides in the charts. With any pesticide, all necessary safety precautions should be taken.

The following four charts present 350 of the most commonly used pest control materials in a practical system based upon a combination of chemical structure and pest control effect.

GLOSSARY OF TERMS AS USED ON THE CHARTS

ALGICIDE - chemical which kills algae

ANTICOAGULANT - rodenticide which kills by interfering with blood clotting

ATTRACTANT - chemical which draws an animal to a place

CONTACT POISON - insecticide which kills upon contacting the outer body surface of an insect

DEODORANT - material masking or destroying odor

EMETIC - chemical causing vomitting; added to rodenticides for safety

EMULSIFIER - chemical which suspends a pesticidal solution in water

FUMIGANT - pesticide which kills upon being inhaled

FUNGICIDE - chemical which kills fungi

HERBICIDE - chemical which kills weeds and other plants

IMPREGNANT - insecticide or repellent infused into clothing or other material

INHIBITOR - chemical which prevents insects from detoxifying an insecticide

INORGANIC - chemical compound not containing carbon

INSECTICIDE - chemical which kills insects and related animals

MOLD INHIBITOR - chemical which prevents mold development in rodenticide baits

NATURAL - found in nature, not synthesized by man

NON-SELECTIVE - kills all types of plants

NON-SUBSTITUTED - organic compound made up of only carbon and hydrogen and sometimes oxygen

ORGANIC - chemical compound containing carbon

REPELLENT - chemical which keeps an animal away from an individual, object or area

RODENTICIDE - chemical which kills rodents and related animals

SELECTIVE - kills only certain types of plants; does not harm other types

SOLVENT - liquid used for dissolving chemicals

SPREADER - substance which distributes pest control chemical through a greater volume

STERILANT - herbicide which kills all plant life in soil

STOMACH POISON - insecticide which kills upon being eaten

SYNERGIST - chemical without pest control effect enhances the effectiveness of a pest control chemical

SYNTHETIC - manufactured by man; not found in nature

WETTING AGENT - chemical which helps suspend a pesticidal dust in water

NOTE: Use of trade names does not indicate endorsement.

THE CHEMICAL CONTROL OF INSECTS

INSECTICIDES

REPELLENTS
- Diethyltoluamide
- Indalone
- Rutgers 612
- Dimethylphthalate
- Dibutylphthalate

ATTRACTANTS
- Geraniol
- Eugenol
- Tetrapinylacetate
- Anethol
- Metaldehyde
- Ammonia
- Saccharine

IMPREGNANTS
- Benzil
- Benzylbenzoate
- Benzocaine
- M-1960
- Mitin
- Eulan
- Beconizer

AUXILIARIES
- Synergists
- Inhibitors
- Solvents
- Emulsifiers
- Wetting Agents
- Spreaders
- Perfumes
- Diluents

Contact Poisons

INORGANIC
- SULFUR GROUP
  - Sulfur
  - Lime-sulfur
- MERCURY GROUP
  - Calomel
  - Corrosive sublimate

ORGANIC

Synthetic
- NON SUBSTITUTED HYDROCARBONS
  - Formaldehyde
  - Metaldehyde
  - b-Naphthol
  - Xanthone
  - Ferbam
- ORGANIC CHLORINE GROUP*
  - Pentachlorophenol
  - BHC
  - Lindane
  - Methoxychlor
  - DDD
  - DDT
  - Dilan
  - Dimite
  - Heptachlor
  - Chlordane
  - Aldrin
  - Dieldrin
  - Endrin
- ORGANIC PHOSPHORUS GROUP
  - Malathion
  - Diazinon
  - Parathion
  - TEPP
  - EPN
  - HETP
  - DDVP
  - Dibrom
  - Guthion
  - Dipterex
  - Entex
  - Bayter
  - Rannel
  - Dicapthon
  - Dimethoate
- ORGANIC NITROGEN GROUP
  - Dinitrophenol
  - DNOC
  - DNOCHP
  - DNOSBP
  - Diphenylamine
  - Azobenzene
  - Karathane
  - Prolan
  - Dinitronaphthol
  - Dinitroanisole
  - Dinitrocresylate
- ORGANIC SULFUR GROUP
  - Aramite
  - Ovex
  - Sulfenone
  - Phenothiazine
  - Genitol
  - Sevin
  - Isolan
  - Dimetilan
  - Pyrolan
- ORGANIC THIOCYANATE GROUP
  - Lethane
  - Thanite
  - Lore

Natural
- PETROLEUM GROUP
  - Fuel Oil
  - Kerosene
- ALKALOID GROUP
  - Nicotine
  - Anabasine
  - Nornicotine
  - Sabadilla
  - Hellebore
  - Ryania
  - Quassia
- ESTER GROUP
  - Pyrethrum
  - Pyrethrins
  - Cinerins
  - (Allethrin)
- ROTENOID GROUP
  - Rotenone
- RESIN GROUP
  - Phellodendrin
  - Croton Oil
  - Amorphin
  - Basil Oil
  - Sage Oil
  - Turpentine

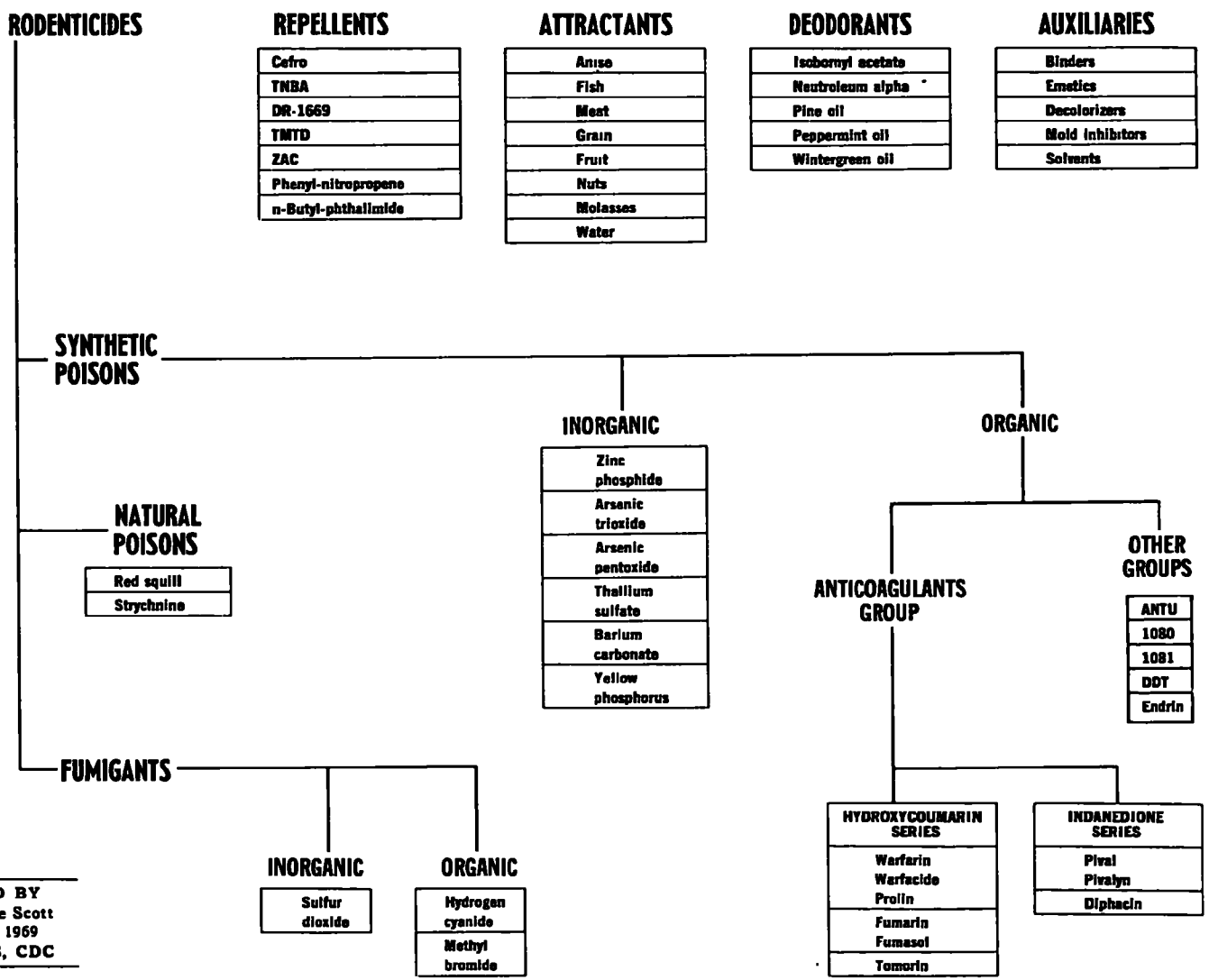
Stomach Poisons
- ARSENIC GROUP
  - Arsenic trioxide
  - Lead arsenate
  - Copper arsenate
  - Paris green
- FLUORINE GROUP
  - Sodium fluoride
  - 1080
  - Cryolite
  - Sodium fluosilicate
- OTHER GROUPS
  - Phosphorus paste
  - Borax
  - Tartar emetic
  - SALP
  - Thallium sulfate

Fumigants
- Hydrogen cyanide
- Methyl bromide
- Carbon tetrachloride
- Ethide
- Sulfur dioxide
- Naphthalene
- o-Dichlorobenzene
- p-Dichlorobenzene

HAROLD GEORGE SCOTT, Ph D.
1962
DHEW, PHS, CDC

*Chlorinated Hydrocarbons

THE CHEMICAL CONTROL OF RODENTS



PREPARED BY
Harold George Scott
REVISED 1969
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CHEMICAL CONTROL OF WEEDS

HERBICIDES

NON-SELECTIVE (SOIL STERILANTS)

ORGANIC

- **SULFATES**: bis (ethyl xanthic) disulfide; DMTT; IPX
- **CHLORATES**: CDAA; dalapon; HCA; PBA; TBA; TCA; TCB
- **MERCURIALS**: mercury acetate; MMAL; MTAL; PMA
- **PHENOLS**: pentachlorophenol; sodium pentachlorophenate
- **UREATES**: DCU; DDMU; diuron; DMU; erbon; fenuron; monuron; neburon; PDC
- **THIOCYANATES**: ammonium thiocyanate; potassium thiocyanate
- **PETROLEUM**: diesel fuel; edeleanu; fuel oil; gasoline; kerosene; stoddard solvent
- **Non-substituted**: acrolein; allyl alcohol; endothal; NPA

INORGANIC

- **SULFATES**: ammonium sulfate; AMS; copper sulfate; ferrous ammonium sulfate; iron sulfate; sulfuric acid
- **CHLORATES**: calcium chlorate; calcium chloride; sodium chlorate; sodium chloride
- **ARSENATES**: arsenic pentoxide; sodium arsenite
- **BORATES**: borax; boron trioxide; sodium borate; sodium metaborate; sodium pentaborate; sodium tetraborate

SELECTIVE

- **CARBAMATES**: CDEC; CIPC; EPTC; IPC; SMDC
- **PHENOXYS**: 2,4-D; 2,5-D; 2,4,5-T; 3,4-D; 4-C; MCPA; sesone; silvex
- **TRIAZINES**: amitrol; atrazine; propazine; simazin; triazine
- **PHENOLS**: DNOC; DNOSAP; DNOSBP

SOIL FUMIGANTS

ORGANIC

- calcium cyanate
- calcium cyanimide
- chlorpicrin
- ethylene dibromide
- methyl bromide
- potassium cyanate

INORGANIC

- carbon disulfide

ALGICIDES

- copper sulfate
- dichlone
- quaternary ammonia
- RADA

INHIBITORS

- ethyl-214
- maleic hydrazide

AUXILIARIES

- buffers
- emulsifiers
- solvents
- spreaders
- wetting agents

WARNING

Weed control via chemicals is a useful method for abatement of mosquitoes and other animal disease vectors, however, herbicides damage useful plants as well as weeds. Some are inflammable. Some require special application techniques. All are toxic to man. Use with care, and follow directions on the label.

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Communicable Disease Center
Atlanta, Georgia

HAROLD GEORGE SCOTT, Ph.D. — 1961

ECONOMIC FUNGICIDES

ORGANIC

HALOGEN COMPOUNDS

Chlorine group

- BHC (p)
- captan (e)
- dichlone (e)
- DDDM (p)
- PCP (p)
- PDB (e)
- phygon
- TCP (p)
- TCQ (p)
- ZTP

Iodine group

- AIT (p)
- EDIT (p)
- BrDIT (p)
- CIB (p)
- CTT (p)
- DITP (p)
- INT (p)
- ITP (p)
- MTIT (p)

Bromine group

- LPB (e)
- LQB (e)

Sulfur group

- thiram (p & e)

Coal-tar group

- carbolineum (p)
- coal-tar

Copper group

- CuAA
- CuN (p)
- CuNPH
- CuQ

Nitrogen group

- ferbam (e)
- maneb (e)
- nabam (e)
- NaDNOC (e)
- PCNB (p)
- quat ammonias
- salicylanilide (e)
- zineb (e)
- ziram (e)

Non-substituted Hydocarbon group

- diphenyl
- glyodin (e)

Mercury group

- aagrani
- calogreen
- ceresan
- ceresan M
- chipcote
- L-224
- mercuran
- mersolite (e)
- merthiolate
- mycon
- N-5-E
- panogen
- PMA (p & e)
- PMU
- sanoseed
- seedox
- semenon
- semesan
- semesan bel
- setrete

INORGANIC

Copper group

- basic copper sulfate
- bordeaux mixture (p)
- copper arsenate
- copper carbonate
- copper hydroxide
- copper oxychloride
- copper phosphate
- COS
- cuprus oxide (p)
- Cu-Zn chromate (e)
- tribasic copper sulfate

Mercury group

- calomel
- mercuric chloride
- mercuric oxide

Sulfur group

- sulfur
- sulfur-lime (p & e)

Zinc group

- zinc oxide-hydroxide

Borax group

- borax (e)

SOIL FUMIGANTS

- CBP (e)
- chloranil
- chloropicrin
- dichloropropene
- ethylene dibromide
- formaldehyde
- HQB (e)
- methyl bromide

(p) – preventive
(e) – eradicative

WARNING

Some fungicides damage plants as well as fungi, some are inflammable, some require special application techniques, and all are toxic Use with care – and follow directions on the label

U S DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Communicable Disease Center
Training Branch
Atlanta, Georgia
WAYNE G BROWN, 1961

SELECTION OF THE PROPER PESTICIDE FOR THE JOB

Harold George Scott

Selection of the proper pesticide should begin with a thoughtful analysis of the objectives of the control program and of the possible ways to achieve that objective. Pesticides may not be a desirable technique. If it does seem advisable to use a pesticide, the exact placement of the pesticide in the control system should be plotted out and the following factors analyzed:

1. EFFECTIVENESS - which pesticides are best able to do the job?

2. AVAILABILITY - which pesticides are readily obtainable?

3. COST - What expenses does each entail in materials, applicator equipment and labor?

4. INITIAL MAGNITUDE - how rapidly do the various pesticides produce what result?

5. EVENTUAL MAGNITUDE - how long do the pesticides last?

6. REACTION - how much resistance can be expected from the pests?

7. SPACIATION - how far from place of application will each pesticide spread?

8. SAFETY - What hazard does each pesticide represent to man? to the environment? What general precautions are needed for each?

9. DISPOSAL - How will empty containers and unused pesticides be disposed of or stored?

10. LEGALITY - what special precautions are needed for your uses? What restrictions exist on the use of each pesticide?

11. COMPETENCE - Do you have properly trained personnel available?

NONCHEMICAL METHODS OF PEST CONTROL

Thomas J. Henneberry

The growing concern of the public and scientists concerning the demonstrated adverse effects of insecticides has stimulated renewed entomological effort to develop effective, efficient insect controls which are compatible with and have minimum effect on the complex components of the agro-ecosystem. The methods of insect control available to the entomologist today are the results of more than one-hundred years of careful observation, experimentation, and creative thinking by scientists concerned with insect control. The present era of pest control using synthetic chemicals began during World War II. The benefits to mankind attributed to the use of these chemicals for insect control is inestimable. However, problems have arisen. Adverse effects on parasites and predators, chemical residues, arthropod resistance to chemicals and high cost and temporary nature of the treatments have been of increasing concern to everyone involved in pest control.

Other methods of insect control; varietal resistance, biological agents, sterility, cultural techniques, repellents, attractants, and many other procedures have long been recognized and recommended by scientists as having potential in insect control programs. The Entomology Research Division of the USDA began to reorient its research program in 1955 from major emphasis on conventional insecticides to more selective chemical and nonchemical methods to control major insect pests[1]. At the present time approximately 16% of the resources of the Division are devoted to insect control using conventional insecticides as compared to 84% in research to develop alternative methods of control and fundamental entomology studies as shown in the tabulation.

MAJOR LINES OF WORK	Percent of Resources By Group	Percent of Resources Subtotals
CONVENTIONAL INSECTICIDES	16	16
OTHER CONTROL METHODS		
Biological control	14	
Insect sterility	12	
Plant resistance	7	51
Cultural and mechanical methods	4	
Attractants, hormones, etc.	14	
FUNDAMENTAL ENTOMOLOGY		
Basic insect biology	19	
Metabolism	2	
Taxonomy	6	33
Insect transmission of plant and animal diseases	2	
Apiculture	4	
		100%

Resistant Plants

One of the most satisfactory methods of preventing damage to plants is through the development of varieties resistant to insect attack. Painter[2] broadly characterized the causes of plant resistance as follows:

1. Preference and Non-Preference
   Plants may not be acceptable to insects for oviposition, food, or shelter because of color, odor, lack of chemical or physical stimuli and/or other similar factors.

2. Antibiosis
   Plants may have an adverse effect on the biology of the insect and in some cases feeding on them may result in death.

3. Tolerance
   Plants may be tolerant to insect attack and sustain numbers that would severely impair or kill more susceptible types.

One of these mechanisms or a combination of all may make plants resistant to attack.

Outstanding achievements have been made in developing wheat varieties resistant to Hessian fly (Myetiola destructor (Say)) and wheat stem sawfly (Cephus cinctus Norton) alfalfa varieties to spotted alfalfa aphid (Therioaphis maculata (Buckton)) and corn varieties to European corn borer (Ostrinia nubilalis (Hubner))[3]. At one time the Hessian fly caused high economic losses in the United States. Today these losses are minimal largely due to the development of resistant wheat varieties. At least 23 are now available to the farmer. Similarly, the dramatic discovery of a solid stem wheat variety which was resistant to wheat stem sawfly resulted in an estimated $4 million annual saving to wheat farmers.

The spotted alfalfa aphid was first discovered in New Mexico in 1954. A crash program was initiated in 1955 and in only 3 years Federal and State scientists working cooperatively developed and released the resistant variety Moapa. Subsequently, many other resistant varieties have been developed. Estimates of savings to the farmer range from $35-70 million annually.

The most destructive pest of corn in the United States is the European corn borer which caused an estimated $350 million damage in 1949 alone. A continuing program of incorporating corn borer resistance in hybrid corn has been a major factor in reducing these losses more than 60% on an annual basis.

Continuing research in all of these programs is essential since experience has taught us that insects can and do change biologically, adjusting and adapting to the types of plants grown in their environment. The identification and incorporation of multiple resistance to an insect pest is especially desirable. If the insect readily adapts to one resistance mechanism, it will probably not adapt to the other, and thus the variety will still be useful.

Often, the level of insect resistance found in commercially useful varieties is not adequate to prevent economic damage by an insect pest. However, such resistance may still be useful because it can reduce the frequency of application and the amount of chemicals required to produce adequate control. This in turn reduces production costs, pollution problems, and may have a sparing effect on parasites and predators.

Research in developing plants resistant to insect attack is a challenging and new area of study. Resistance to pests exists throughout nature and needs only to be discovered, identified, and applied to solve many of our serious pest problems.

Sterility Methods

Methods of using induced sterility to control or eradicate insect populations are among the most significant recent contributions to entomology. The best known, the method of sterile insect release, involves the sustained overflooding of native populations with sterile insects of the same species at densities that are high enough so little probability exists of fertile native matings. The method was hypothesized about 1937 by Dr. Edward F. Knipling, Entomology Research Division, U.S. Department of Agriculture. Then, after many years of research, it became scientific fact when screw-worm flies, Cochliomyia hominivorax (Coquerel), sterilized by irradiation with cobalt-60, were released at the rate of 800 per square mile on Curacao Island in the Netherlands Antilles in 1954. Eradication was complete about 3 months after the first release[4]. Subsequent releases of sterile screw-worms in Florida (The Southeast Screw-Worm Eradication Program) and in the Southwest were similarly successful[5,6]. Expenditures in the Southeast screw-worm sterile release program were less than $10 million, and the estimated savings to cattle growers in that area since its conclusion probably exceed $100 million. In the Southwest program the investment is about $20 million, but livestock men estimate savings of as much as $400 million.

A second method, chemical sterilization of insects, is now being investigated. Chemicals that have sterilizing effects on insects have been known for many years. However, interest in their potential in insect control programs was renewed when the screw-worm eradication campaigns were successful and LaBrecque[7] found 3 alkylating agents that induced sterility in both sexes of house flies, Musca domestica (L.). If effective methods of using these sterilants can be developed, it is possible that they can be used both to sterilize insects for mass releases and also to sterilize a native population.

The Method of Sterile Insect Release

Suppression of insect populations by the method of sterile insect release requires the mass rearing of the subject species, the inducing of sterility, and the sustained release of the sterile insects into the wild population in such numbers that the probability of a fertile native mating becomes progressively more remote as the releases continue. This constant pressure on reproductive potential results in a marked decrease in and theoretical elimination of the insect population within a relatively few generations.

For example, Knipling's[8] calculations indicate that when 90% of the total insect population in the first generation consists of released sterile insects and the same number of sterile insects are released each subsequent generation, the native population will be eliminated by the fourth generation. In contrast, a program of control with insecticides which kills 90% of the insects in each generation would theoretically require more than 10 generations to eliminate the population. The initial effect of both systems is the same, but the sustained release of sterile insects each succeeding generation has a progressively greater effect on the reproductive potential of the native population; applications of insecticides produce a constant pressure each generation and therefore require more than 2.5 times as long to produce the same total effect.

The essential prerequisites that must be satisfied for the elimination of a particular insect include an efficient method of mass rearing, techniques of sterilization that have no adverse effects on the mating capability, competitiveness, or vigor of the species, a practical and efficient means of disseminating the sterile insects into the native environment, and assurance that the released insects will not create undue hazards or loss to crops, livestock, or man[8].

Another essential prerequisite is that the initial releases of sterile insects must produce high enough overflooding ratios of sterile to native insects to start a downward trend in the population. Information about the distribution of the native

population and quantitative and qualitative information about the population density, particularly at the low cycle of the population, is therefore essential. Sterile insect releases are highly efficient when the population is small; conventional insecticides are least efficient against small populations and highly efficient when populations are large. Thus, the optimum time to begin a program of sterile insect releases is when the active native population is at its lowest level, and the proper timing for all releases must be critically and exactly determined.

Also, a sterile insect release program will be effective only when the reproductive potential of the total population, or of a large segment of it, is suppressed. Since many insect species are capable of moving great distances, the full effect of the technique can probably only be fully demonstrated on isolated populations unless the migration of native insects into the experimental areas can be greatly reduced or prevented.

Sterilizing Native Populations

If chemical sterilants could be used to sterilize insects in a native population, the expense of mass rearing and releases would be eliminated and the sterilized insects would remain in the population to compete sexually with unsterilized native insects. This latter effect would be a bonus and would further reduce the reproductive potential of the native population. For example, if an insecticide kills 90 of 100 insects of each sex in a population, 10 pairs will remain to mate and produce the next generation. If a sterilizing agent renders 90 of 100 insects of each sex in a population incapable of reproduction, the 10 males that avoided the sterilant compete in mating for the 10 remaining females with the 90 sterilized males. We would expect only 1 fertile mating to result from this combination. Moreover, the sterilized population would compete in time and space in the insects' ecosystem[9]. The use of chemosterilants with various baits and attractants appears a promising method of inducing sterility in native insect populations.

Knipling and McGuire[10] developed seven hypothetical population models to evaluate the potential of sex attractants in insect control programs. Essentially, their findings indicated that: (a) a trapping or appropriate system of treatment in which the ratio of the equivalents of the competing sex attractant (synthetic, extract, or caged virgin females) to the number of wild females in the population was high would greatly reduce the probability of native male matings; (b) the total impact of the system of treatment on the reproductive potential of the population would not be affected by the number of matings attempted by males but would increase if females were attracted to male attractants and attempted multiple matings before oviposition; (c) killing the attracted males would be only slightly less effective than sterilizing them; and (d) the most efficient system of sterilizing a native population would be realized if both sexes were attracted and sterilized. The authors also indicated that releases of sterile males combined with the use of baited chemicals (sex attractants) that would kill or sterilize the native males would substantially increase the degree of population control. In addition, they showed that theoretically the use of a given number of caged virgin female insects as sex attractants would be as effective as the release of the same number of sterile males; also, they would achieve the same increasing degree of effectiveness as the native population declined as would releases of sterile insects.

The theoretical considerations are challenging, and the tremendous potential of integrated methods of inducing sterility deserve extensive consideration by researchers to evaluate their merit.

Sterility methods have been shown to have a high degree of potential for many economic insect species. For example, the potential of the method was demonstrated with the codling moth, Carpocapsa pomonella (L.), in limited field trials[11,12]. In a test in 1966, chemically sterilized codling moth males were released by the USDA Entomology Research Division in a 15-acre apple orchard at Yakima, Washington. The results were promising and the control obtained was as good as that obtained in orchards treated with the regular schedule of insecticidal sprays. In addition, the absence of the sprays permitted the natural predators and parasites to provide effective control of

the European red mite, Panonychus ulmi (Koch), and the wooly apple aphid, Eriosoma lanigerum (Mausmann). Similar results were obtained with releases of irradiated codling moths in Canada in 1966 and at Yakima in 1967 in a 93-acre apple orchard (Butt, personal communication).

Before area-wide population control of the codling moth by the method of sterile insect release can be proved feasible and practical, a large-scale pilot program involving several thousand or more acres must be conducted. Such a project would bridge the gap between exploratory research and practical application.

The development of techniques of controlling insect populations by the method of sterile insect releases over large areas is a tremendous undertaking. The talents of many scientific disciplines are involved, and the most detailed and exacting information concerning rearing, biology, ecology, behavior, and population dynamics of the subject species is required. However, when the procedure is successfully developed and implemented, it can substantially reduce insect losses and the costs of control and can avoid the introduction of damaging side effects into our environment.

Biological Control

Biological control agents are the most important factors in regulating natural populations of noxious insects. More than 1,100 viruses, bacteria, fungi, protozoa, rickettsia, and nematodes attack insects in their environment[13]. Viruses attack eighteen or more important crop pests such as the corn earworm, Heliothis zea (Boddie), the cabbage looper, Trichoplusia ni (Hubner), the tobacco budworm, H. virescens (F.), and the armyworm, Pseudaletia unipuncta (Haworth).

Spectacular results were obtained when viruses were used to control certain forest insect pests[14], and a bacterial pathogen, Bacillus popillae Dutky, that attacks Japanese beetles, Popillia japonica Newman, provides good control of this insect[15] when it is applied as a spore dust to turf. Another bacterium, Bacillus thuringiensis var. thuringiensis Berliner, is pathogenic to about 110 species of Lepidoptera and 8 species of Diptera[16] and is recommended for control of cabbage loopers, alfalfa caterpillars, Colias eurytheme Boisduval, and the tobacco hornworm, Manduca sexta (L.).

A number of formulations or varieties of Bacillus thuringiensis have been tested for insect control. A strain has been found which, under laboratory conditions, is about 100 times more effective than strains commercially available against the bollworm on cotton and against other insect pests[17]. The effectiveness of this new strain, referred to as HD-1, must be determined under field conditions before its practical value can be appraised. However, field studies to date are most promising. Other field studies have shown that a polyhedrosis virus for control of cabbage looper is just as effective and economical as insecticides. Another polyhedrosis virus has sometimes afforded the same high degree of control of the cotton bollworm. Variations in test results with insect viruses are believed to be due to the way in which they have been formulated, and efforts are being made by industry to develop improved and more stable formulations. Like chemical pesticides, much toxicological data will be required to prove the safety of an insect virus before it will be registered and receive approval for use.

Control of agricultural pests by parasites and predators has also had some marked successes[18]. One aspect of the use of insect parasites and predators for insect control involves exploration, introduction, evaluation, distribution, and establishment so that they will become a part of the environment and contribute to the control of destructive insect pests. Another aspect is to protect native beneficial insects which play a very important role in regulating destructive pest populations. Attempts have been made to introduce parasites and predators of about 80 pests into the U.S. over a span of more than 80 years[19,20]. Of about 520 species that have been imported, 115 have become established, but only about 20 have provided important control of some of our worst pests. Introductions of beneficial insects have proved quite useful against several scale insects, the European corn borer, gypsy moth (Porthetria dispar (L.)),

alfalfa weevil (Hypera postica (Gyllenhal)), Rhodes-grass scale (Antonina graminis (Maskell)), and others. One approach that deserves considerable attention is the possibility of mass rearing insect parasites and predators for sustained release to supplement the native forms in the environment.

The possibility is now being investigated in the Blue Mountain area of Washington where large acreages of canning peas are grown and pea aphids, Acyrthosiphon pisum (Harris), are a problem. The pests overwinter on alfalfa plants that are also reservoirs of pea enation and pea streak viruses, and then the alate aphid forms migrate to peas in the spring[21]. About 100 million braconid parasites, Aphidius pulcher Baker and Aphidius smithi Sharma and Subba Rao, were therefore reared and released in the spring of 1966 to determine the effectiveness of these parasites in controlling the populations of pea aphids developing on the alfalfa. Also, portable polyethylene-covered greenhouses were developed and placed over dormant alfalfa in the winter to protect the plants from the weather and to force growth four to six weeks ahead of the alfalfa in the surrounding fields.

These field nurseries were then stocked with laboratory-reared pea aphids and parasites. As the populations of parasites in the cages developed, they were allowed to escape through temperature-controlled automatic roof vents[22]. The results to date indicate that substantial control of pea aphids on alfalfa was obtained with subsequent reduction in migrations to pea plantings. The possibility of controlling pea aphids by this method appears promising.

Field tests have shown that two mass releases totaling 292,000 predatory aphid lion, Crysopa carnea Stephens, eggs or larvae per acre was as effective against the bollworm on cotton as the best available insecticides[23].

Attractants

Insects respond positively to many chemical, biological and physical stimuli. Entomologists have visualized the potential of manipulating the resulting behavioral responses to achieve economic control of pests through trapping and killing, luring and sterilizing, or disrupting their mating behavior.

The most potent and specific insect attractants appear at present to be the sex pheromones, and Jacobson[24] recently compiled a list showing that such pheromones have been demonstrated in more than 200 insect species.

At present, we have completed the isolation, identification, and synthesizing of the sex pheromone of only a relatively few insects. One of the most recent was that of the cabbage looper[25]. However, while the chemists were still working to produce the synthetic pheromone, researchers were using living female moths to investigate possible ways of using the attractant when it was ready.

One of the first approaches was to combine living virgin female moths and a trap equipped with a blacklight lamp which is known to attract and catch cabbage looper moths. When the two attractants were combined to produce a baited trap, more male insects were captured in the baited traps than in traps equipped with either blacklight or virgin females alone[26]. Thus, when the breakthrough in synthesis came, investigators were ready to evaluate the potential of the synthetic pheromone in the field[27].

A ranch near Red Rock, Arizona, that includes 3,110 acres, 2,240 acres of which are in crops, was selected for the test. (Annually about 1,000 acres are planted to fall lettuce, 800 acres to spring lettuce, and 200 acres to cotton.) The installation of blacklight traps baited with synthetic cabbage looper sex pheromone at the rate of about one trap unit per six acres of cultivated ground was completed in March 1966. To date, collections of female cabbage looper moths in a check area about nine miles

away have been 14 times greater and catches of male cabbage loopers have been 30 times greater than in the control lighted area. Also, though egg and larval counts have varied considerably, fewer eggs and larvae were found on lettuce in the trapping area compared with the check area. Thus, the results appear promising though the intensive use of insecticides on the ranch makes it impossible to evaluate the full impact of the baited traps.

Since 1966, research has been conducted on the island of St. Croix, U.S. Virgin Islands to evaluate the effects of traps equipped with blacklight lamps on populations of the tobacco hornworm. The approximately 3 traps per square mile installed on the 84-square-mile island became operational in June 1967. However, for about 1 year before the lights were turned on, 9 separate traps were operated to develop baseline information on the magnitude and seasonal distribution of the populations. Also, in 1968 after Hoffman et al.[28] demonstrated that baiting light traps with virgin female hornworm moths resulted in marked increases in the catch of males, all the light traps on the island have been baited with virgin female moths.

Since the traps began operating, the populations of tobacco hornworm moths have decreased consistently; in March 1968, they appeared to be about 30-40% as high as the populations recorded before the experiment. Also, after the traps were baited with virgin female moths in March 1968, the male catches increased about 6-10 times in the baited traps compared with the catch in unbaited traps. Moreover, for about 6-8 weeks after the first baiting of the light traps, 4-5% of the females collected in the traps were unmated. This percentage increased to about 6-10% for several months to a peak of 30% virgin females and declined thereafter to a relatively constant rate of 14-16% unmated females. Another indication of the effect of baited traps on populations of male hornworms is the decrease in the percentage of males caught in unbaited traps from a fairly constant 60% before the baiting to about 40% at the present time. Thus, the population of tobacco hornworms on the island of St. Croix, measured by catches in the light traps, now appears to be about 20% of that present on the island before the beginning of the experiments (W. Cantelo and J. Smith, personal communications). The results are in the preliminary stages of evaluation, but we hope they will provide us with some answers about how light traps can fit into programs for control of hornworms.

The possible use of sex pheromones in preventing orientation or through mating inhibition is also an exciting new concept.

One phenomena that has been observed by investigators studying male behavior after stimulation by sex pheromones is adaptation or attenuation of response after prior conditioning stimulus. The threshold concentration of pheromone necessary to induce response is raised for a time following the period of exposure. Cabbage looper males may not respond to a given threshold concentration for several hours after first exposure to the pheromone[29,30].

Many investigators have proposed that if high enough concentrations of pheromone were maintained over large areas, native females could not contribute enough additional pheromone to result in orientation to them and males would never locate females to inseminate them. Under field conditions a concentration of 1×10^{-10} g/liter completely prevented orientation of males to pheromone-emitting females[31].

The potential of an attractant combined with a toxicant to provide low-cost control of a pest over a large area was demonstrated when the oriental fruit fly, Dacus dorsalis Hendel, was eradicated on the island of Rota[32]. Methyl eugenol, a powerful male attractant, was combined with 1% naled and impregnated in cane-fiber squares. The squares were dropped from aircraft flight lanes about five miles apart, except for inhabited areas where bait stations were used. Daily monitoring with traps showed an immediate 93% reduction in fly populations. After 10 drops, no flies were captured and none have been found during the 24 subsequent months of trapping and inspecting of host fruits. Only 3.5 grams of toxicant/acre were required for the entire program.

Repellent Techniques

Although great progress in insect control has been made with insecticides, these killing agents do not prevent viruliferous insects from infecting crop plants; such vectors must be killed almost instantly or prevented from feeding.

Numerous investigators have observed and reported on the response of aphids to color and light[33,34,35]. Also, the repellent effect of aluminum foil on insects was first observed in 1949 by Lester Wall, Reynolds Metal Co., Richmond, Virginia (unpublished report), and Kring[36] reported that when unpainted aluminum pans were placed around yellow pan traps, aphids avoided the yellow pan traps. Smith[37] therefore began tests in 1963 at Beltsville, Maryland to determine whether this phenomena could be used to repel flying aphids and reduce incidence of viral infections in crops.

In one test in 1965, 50% of the soil area of each field plot of bush squash at Beltsville, Maryland was covered with sheet aluminum foil. Other plots were untreated or sprayed with an effective aphicide. The presence of the aluminum sheets reduced the catch of aphids by more than 95% compared with the catch in unmulched check plots and in plots sprayed with an insecticide during a 3-day period of heavy aphid flight. Also, the number of infected plants in the mulched plots was greatly reduced for 6 to 7 weeks compared with virus infected plants in the sprayed and untreated plots, and the yields of squash in the mulched plots were 6 times greater[38].

In another test at Long Island, New York, mulches of reflective aluminum and also of white plastic reduced catches of winged aphids in yellow pan traps by more than 87% and decreased the spread of cucumber mosaic virus in gladiolus plantings[39]. Other researchers who have used such a mulch have reported reduction of lettuce mosaic in lettuce plots[40] and protection of roses from flower thrips, Frankliniella tritici (Fitch), injury[41]. Aluminum mulches have not been effective with all aphids on all crops[42,43]; however, reflective mulches with plastic or paper backing can be produced to a wide range of specifications, and growers of some commercial crops are trying such mulches to warm the soil early and to achieve control of weeds and aphids.

Insect Hormones

Another recent trend is research on insect hormones and hormonelike materials that disrupt insect development rather than to cause immediate death. Sterility in adult insects may result soon after treatment with molting hormones or their analogs, whereas juvenile hormones act by interrupting insect development and in some cases produce monster insects that finally die or, should they attain adulthood, cannot reproduce because of their physical abnormalities[44]. Some of these hormonal materials, which would not be expected to have a detrimental effect on nontarget organisms, are effective against test insects at small dosage rates, about 1 nanogram or one-billionth of a gram. New "hybrid" synthetic ethers, which are juvenile-hormonelike materials, have been found to block normal insect growth and development. These compounds, some of which are fairly easy to synthesize, often show greater potency than the insects' own hormones or biologically similar synthetic compounds previously tested[45].

Cultural Techniques

In the Pacific Northwest, the green peach aphid is also the most important vector of beet western yellows and beet yellows viruses, diseases that cause annual losses of as much as 25 to 30% of the yield of sugarbeets[46]. Also, unfortunately, beet western yellows, the most prevalent of the yellows diseases there, can be harbored by 30 or more hosts other than beets which serve as reservoirs of the virus[47]. As noted, the

green peach aphid overwinters primarily in the egg stage on peach trees in the general area, but small numbers of the summer forms overwinter and feed on plants growing year-round in protected places, and intensive ecological studies made between 1962 and 1964 showed that many of these overwintering hosts of the summer aphid forms were also alternate hosts of beet western yellows virus[48, 49]. Also, warm spring-fed drainage ditches in sugarbeet-growing areas near Toppenish, Washington proved to provide a micro-climate 20-50°F. warmer than the surrounding environment where the weeds and aphids could fluorish throughout the year. Thus, though aphids from eggs overwintered on peach trees are free of virus until they feed on diseased plants, the summer aphid forms that overwinter on infected weeds carry the virus to young sugarbeet plants when they migrate to them in the spring.

These findings stimulated studies to determine whether eliminating overwintering populations of aphids and weed hosts from drainage ditches would reduce viral infections in nearby sugarbeet fields. A 22- and a 30-square-mile area southwest of Toppenish, Washington that contained 42 to 53 miles of drainage ditches were the test areas; a similar area 4 miles east of the experimental area served as a check. During January, February, and March 1965-1967, before sugarbeets began growing and aphids began migrating, the weeds in the drainage ditches in the test area were destroyed by burning. In 1966, 91% fewer aphids and 76% fewer diseased plants were found in the area where the ditches were burned than in the unburned check areas; in 1967, 75% fewer diseased plants were found in the burned area than in the unburned check area. The increased yield in the test area was estimated at more than 2 tons per acre, and the cost of ditch burning per acre of sugarbeets protected ranged from $2.20 to $6.85 and averaged $4.00 for the three years. This cost compares favorably with the average estimated cost of $16.00 per acre for conventional chemical sprays.

The results of this research have been received enthusiastically by the sugarbeet-growing industry and the individual growers in the area, and they have now contracted to have the ditch burning done on a routine basis as part of their regular process of insect control.

Another example of the method of host elimination or replacement to reduce an insect population concerns the beet leafhopper, Circulifer tenellus (Baker), in Idaho. This insect is the sole known vector of curly top virus in the United States, and the large desert and range areas in southern Idaho where weed-host plants (several species of broad-leaved annual plants) have become established and serve as overwintering and spring hosts. (Russian thistle is the most important summer host.) Scientists recognized that the breeding areas proper might be the vulnerable link in the host-plant cycle and postulated that if it were broken, effective control of the insect could be obtained. (The acreage of Russian thistle is smaller than that of annual weed hosts and appeared more vulnerable to control.)

The Bureau of Land Management, Department of the Interior, therefore began seeding the summer breeding areas of the beet leafhopper in Idaho in 1959 with crested wheatgrass, Agropyron cristatum (L.) Gaertn. The cost per acre of this seeding ranges from $3.25 to $6.00 per acre depending on the method used. Also, the Plant Pest Control and Entomology Research Divisions, Agricultural Research Service, U.S. Department of Agriculture, and the Idaho Bean Commission have cooperated in advisory capacities. Since the program began, permanent crested wheatgrass has been seeded over more than 200,000 acres of range[50,51].

Before the seeding program began, curly top virus caused losses in sugarbeet yields of as much as 65%. Also, the beet leafhopper transmitted the virus to beans, tomatoes, and other agriculturally important crops. Since the initiation of the program, the situation has changed remarkably. Curly top has been reduced to a minor problem, and the establishment of crested wheatgrass has increased the carrying capacity of range

for annual grazing tenfold, in addition to increasing the dependability of available range forage and reducing the hazards of grass fires and wind erosion[51]. Thus, the outcome is a fine demonstration of an effective, economical, and efficient method of controlling an insect through the application of many scientific disciplines to the solution of a common problem.

Integrated Control

Integrated control is a system designed to use all available, suitable, and necessary methods of controlling insects to reduce pest populations and maintain them at levels below economic thresholds. The development of integrated control systems are based on exacting and definitive information on the biology, ecology and population dynamics of the pest species in the complex agro-ecosystem being considered. Although literally hundreds of insects may occur, there are usually 1 or 2 major insect pests which cause economic damage. These are the key species which must be controlled with minimum or no effects on the other complex components of the ecosystem and their interactions. Pickett and McPhee[52] were among the first to recognize the adverse effects of the unilateral chemical approach to ordered pest control and they developed valid principles for an integrated control program which has provided guidelines and influenced the direction of subsequent research.

The majority of entomologists recognize the mistakes of the past. Recognizing the variety of methods of insect control now available, it is imperative that all consideration be given to developing logical, effective and efficient systems through combinations of these methods. Thus, we can bring maximum pressure on pest insect populations while minimizing the impact on the entire agro-ecosystem.

Summary

Research designed to develop and exploit alternative nonchemical methods of insect control demand the most exacting and sophisticated information on insect biology, behavior, movement, ecology, and population dynamics. The focus of research must be directed at an entire key insect population, or a large segment of it, since these methods are designed to suppress or reduce the insect population to a level below its economic threshold. Many insect species are capable of moving great distances and methods designed to reduce such populations in local or very limited areas have a low probability of success because insects migrating from great distances often prevent successful reductions of the total population in the management area.

In recent years there have been a number of significant successes in the application of nonchemical methods for insect control. However, no one method appears to be adequate to solve all insect problems or even, in many cases, the same insect problem under different ecological conditions. In many cases, there may not be a single method which will accomplish effective control but a combination of methods which are logically and effectively integrated may be required to bring maximum pressure on an insect population.

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THE DIAGNOSIS AND TREATMENT OF ACUTE PESTICIDE POISONING CASES

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Pesticide poisoning is reported by the National Clearinghouse for Poison Control Centers at about 5,000-6,000, cases per year. This represents, for the most part, accidental poisoning among children. Many more cases than this occur, especially among pesticide exposed workers, but there are few reports of these. The fatality rate in pesticide poisoning is considerably higher than that seen with the more common agents in poisoning such as aspirin, tranquilizers, and birth control pills.

The incidence of pesticide poisoning varies a great deal from region to region in the U.S.A., being highest in agricultural areas and in urban centers surrounded by agricultural areas.

Poisoning at times occurs on a mass scale when flour, sugar, or the like, become contaminated with pesticides in transit or in storage, since pesticides survive the cooking and baking processes quite well. Examples of these are the food poisoning episodes of recent years in the Middle East, Columbia, and Mexico. Episodes on a much smaller scale have occurred in the U.S.A.

The Community Studies have been conducting prospective epidemiological studies of workers exposed to pesticides to determine if their health is being adversely affected. In addition to this, our Studies provide diagnostic and therapeutic assistance in their local areas to Doctors handling cases of acute poisoning. Most of our reports to date have come from south Texas and South Florida which represent primarily cases of individual poisoning but at times are of group poisoning.

In south Texas, the incidence of poisoning increased for several years, then declined only to rise again. Most cases occurred in June and July during the period of greatest pesticide use. Most cases were among teen-agers and young adults who were employed by farmers and spray pilots to assist in mixing and applying pesticides. Parathion and methyl parathion were the usual agents, and the route of exposure was almost always dermal. Very few deaths occurred, even though pesticides are by far and away the leading cause of poisoning in this area.

The signs and symptoms observed in these cases indicate that a variety of biochemical and physiological functions are altered by pesticides. The central nervous system, cardiovascular system, gastrointestinal system, and musculoskeletal system are the most obviously affected in pesticide poisoning. The diagnosis may be difficult, because of this variety of signs and symptoms which are suggestive of other conditions as well as pesticide poisoning.

In south Florida, poisoning reflects three sorts of circumstances: (1) accidental ingestion by 1 to 2 year old children in and around the house; (2) accidental dermal exposure in occupational exposed workers; and (3) suicidal ingestion in middle-aged to older adults. Numerous pesticides have caused deaths in this area, ranging from old types like Paris Green up to newer pesticides like Zectran. In Florida, pesticide poisoning is a year round phenomenon rather than coinciding with the season of greatest agricultural use of pesticides. This is due to the importance of the accidental cases among children and the suicidal cases among adults. The highest death rates are among adults, but this represents the fact that such a large proportion of these are suicidal. The agents of most importance are the organophosphates, especially parathion, but numerous compounds singly or in combination have been involved. There have been several homicidal attempts with pesticides too, most of which have been successful. In this area, the leading cause of death from poisoning among children is pesticides.

How important pesticide poisoning is in your area will depend upon several factors already noted. Determining what the true incidence is in any particular area may be difficult, because of errors in diagnosis and the lack of an effective system of reporting. Such poisoning is, however, preventable -- though suicidal cases present particular problems.

When one considers that only about 10% of the true incidence of poisoning in the U.S.A. is reported, and that the Poison Control Centers report over 100,000 cases per year, it is apparent that poisoning (not just with pesticides) represents an important public health problem.

CHRONIC BIOLOGIC HAZARDS OF PESTICIDES

MUTAGENESIS

Stanley Glenn

Mutagenesis deals with the capability of producing genetic damage. When genetic damage occurs, the burden of hereditary defects in future generations is increased. One potential genetic hazard comes from pesticides; however, the overwhelming majority have not been adequately tested, although appropriate techniques and methods are now available.

The word mutation is used to designate any inherited change in the genetic material. It may be a chemical transformation of an individual gene that causes it to have an altered function, or the change may involve a rearrangement, or a gain or loss, of parts of a chromosome. This kind of change is often visible by ordinary microscopy. Mutations may occur anywhere in the body, and frequently the result is the death of the cell involved. A mutation that is transmitted via the sperm or egg to the next generation can affect every cell in the body of the descendent individual, with consequences that can be disastrous.

What kinds of effects on the human being do mutations produce? The most important fact to emphasize is that there is no single effect, for the range of effects produced by gene alterations includes every type of structure and process. At one extreme are consequences so severe that the individual cannot survive, so-called lethal effects. If death occurs early in embryonic development, it may never be detected. If death is at a later stage, it may lead to a miscarriage. Roughly one-fourth of spontaneous abortions show a detectable chromosome aberration. If the embryo survives until birth, there may be physical abnormalities. There are hundreds of known inherited diseases and probably many more that are unknown, all of which owe their ultimate cause to mutations.

At the other extreme are genes with mild effects, and those with smaller effects finally become imperceptible.

Some mutant genes are dominant, in which case the abnormality or disease will appear in the very next generation after the mutation occurs. If the gene is recessive, the disease or abnormality may be delayed for many generations until some unlucky child inherits a mutant gene from each of his parents. What happens in the first generation is only a fraction of the total impact of the mutation process. If the gene causes a lethal or sterilizing effect, it will

persist for only one generation and will affect only one person. If it causes only a slight impairment, it may be transmitted from generation to generation and thereby affect many people.

The first evidence in 1927 that environmental agents under human control might have some influence on the genetic constitution of future populations followed the discovery that high energy radiation causes mutations. The discovery of nuclear energy brought a whole new dimension to the problem and greatly increased public awareness of genetic hazards. As soon as radiation-induced mutagenesis was discovered, there were strong reasons to suspect that many chemicals might have the same effect, but proof of this did not come until after World War II when mustard gas was shown to induce mutations in fruit flies. Since that time a large number of chemicals of a great diversity of structure and activity have been shown to be mutagenic. Pesticides are of particular concern because they are used so widely and in such enormous amounts; they are very potent biologically... otherwise they would not be effective pesticides.

There are approximately 55,000 pesticides on the market at the present time made up of various combinations of 400 basic chemicals. Certain of these pesticides have been clearly shown to have mutagenic characteristics. Despite the extensive use of pesticides, our information on their possible mutagenicity is grossly inadequate. Several have been tested in various test systems, but the Mrak Committee believes that none have had the kind of testing that would be regarded as adequate. An important area is the effects of exposure to combinations of compounds. The possibility of pesticides potentiating other pesticides or other chemical agents to become mutagens has not been explored.

A variety of test methods are available, and the mammalian test systems have the greatest relevance to human problems. In addition to the test procedures, human population monitoring may reveal mutagenic effects of pesticides or any other environmental agents that have escaped detection. The task of setting up a system of population monitoring would be terribly difficult; the damage caused by mutations occurs in future generations, not in this one, so the effect would not be observed for some time.

For the present, we have to accept the fact that any feasible system of monitoring the human population could detect only a very gross effect.

As far as predicting mutagenesis is concerned, chemical structure can be a useful guide. For example, many alkylating chemosterilants could have been predicted to be mutagenic in advance of actual tests. If

priorities are needed in testing, those pesticides that are used in the largest amounts should be placed at the top of the list, with the greatest emphasis on those used domestically and on food crops. Particular attention should be directed to domestic exposure by inhalation of pesticide aerosols and vaporizing pesticide strips.

Literature dealing with mutagenicity of pesticides comprises more than 500 papers. Captan has been tested and found to be mutagenic by a variety of techniques. Preliminary studies by Legator (1970) indicated that p,p' DDT is capable of inducing dominant lethal mutations in rats. Palmer et al (1970), using tissue cultures of rat-kangaroo cells, found that the p,p' forms of DDT, DDD and DDE produced twice as many chromosome breaks as did the corresponding o,p' forms. Tsanebara-Maneve et al (1969) produced chromosomal aberrations with the organophosphate diazinon in human lymphocytes in culture.

Mutagenicity is becoming increasingly important to humans as life expectancy is lengthened through control of parasitic and bacterial diseases, morbidity from genetic weaknesses caused by mutation is increasing. Mutational effects may continue for many generations after the mutation has occurred.

Genetic impairments already account for a very large part of our existing burden of disease and premature death. If proper weight is given to the genetic component of many common diseases, we can calculate that at least 25% of our health burden is of genetic origin. This figure is a very conservative estimate in view of the genetic component of such griefs as schizophrenia, diabetes, atherosclerosis, mental retardation, early senility, and childhood malformations. With the reduction in morbidity of infectious diseases, there will be an increased percentage of health effects due to genetic causes, until they approach the level of accident-induced traumas.

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CHRONIC BIOLOGIC HAZARDS OF PESTICIDES

TERATOLOGY

Burton R. Evans

Introduction

Teratology is the study of congenital malformations. These malformations or abnormalities occur in live fetuses, and practically all such effects occur during embryonic organ development.

The magnitude of teratogenesis or congenital malformations should be put into proper perspective. It presents obvious personal, financial, medical and social stress on the individual and the community. "One-third of the beds in children's hospitals today are occupied by individuals with congenital defects... One survey indicates that 4 to 7.5 percent of human deliveries yield offspring that have developmental defects which will interfere with survival or result in clinical disease within the first year of life."[3]

Early attempts to explain congenital malformations varied and are still heard today. There is the "Wrath of God"--or you are being punished for doing something wrong, or the mother's mental impressions during pregnancy would have some influence on the child's development. As late as 1965 there was a report of the execution in a Near East country of a mother for producing a child with a well developed-tail. She was charged with consorting with a monkey![2]

The science of experimental mammalian teratology began in the 1930's. Malformations were experimentally produced in animals by x-rays and Vitamin A deficiency. Rubella was identified as a teratogen in 1941.[2]

The famous thalidomide disaster of the early 1960's accelerated the interest in the teratology of drugs. In 1968 the so-called "Bionetics" screening study which investigated the teratogenic potential of a number of widely used pesticides stimulated investigations in this area. In 1969-70 discovery of high levels of methyl mercury in fish of the American rivers, bays, and lakes spurred interest in the teratogenic effects of this compound. The Japanese had had this problem during the years of 1953-58 (Minamata Bay disease) and in 1964-65 (Niigata disease).[1]

Problems in Teratology Research

Since the thalidomide episode, teratogenicity testing has been required before approval for use of a new drug is given by FDA. Since testing can not obviously be done on man, this raises practical problems as to the test animal. Unfortunately, no other animal parallels the teratogenic response observed in humans. For example, cortisone and thalidomide will cause malformations in the humans as well as the mouse, but have no effect on several strains of rats. On the other hand, substances in wide use by humans, such as adrenalin, insulin, salicylates and certain antibiotics, are all known to cause teratogenesis in laboratory animals but not in humans. Despite those problems, the rat, rabbit, hamster and mouse are the most common test animals used. Extrapolation from animal to man is always a problem. In practice, the usual teratogenic agents (x-rays, German measles, thalidomide and mercury) were each recognized by an alert medical practitioner who observed a cluster of unusual cases and traced the cause to its source.[3]

In determining a teratogenic effect, the time of administration, the route of administration, the dose level, the number of doses and the presence of additional stress (i.e., nutritional deficiency) and the species used in the test animal all play a role. For example, the most susceptible period is when the germ layers are forming, in humans this is in the first three months of pregnancy. It is, therefore, obvious that by adjusting one or more of these factors, teratogenesis could theoretically be produced with almost any substance.[4]

Interactions in Teratology

Malformations may be caused by genetic or chromosomal aberrations and be inherited in some families, such as cleft palate, clubfoot, etc. Nutritional deficiencies are known to cause some abnormalities, such as a lack or inability to use Vitamin D induces embryonic rickets. Lack of iodine, or its excess, may cause brain damage. X-rays are known to produce congenital malformations. The potential danger from such as thalidomide, are well known.

Pesticides and Other Chemicals

Within the last two years the teratogenicity of pesticides has evoked interest because of the screening study, carried out by Bionetics Research Laboratories under a contract for the National Cancer Institute (58) which involved a number of widely used pesticides and fungicides. The work of this laboratory, plus the work of many other researchers have shown that under certain conditions a few pesticides will cause teratogenic effects on some animals, such as paraquat in rats (costal cartilage malformations), and carbaryl in the guinea pig.[4] Particular attention has centered upon the chlorophenoxy compound 2,4,5-T because of its widespread military use as a defoliant in Viet Nam. Recent findings with the herbicide 2,4,5-T have shown the teratogenicity of this substance is due to in part to a contaminant, "dioxin."[4] Abnormal fetuses (cleft palate and cystic kidneys) were found in two strains of mice.

Herbicides applied, including some 2,4,5-T, to the Tonto National Forest in 1969 near Globe, Arizona, for the control of chaparral on 1,900 acres raised a storm of protest from local citizens. Deformities in the human and animal population were charged, in addition to the loss of livestock and crops.[7] An investigating panel consisting of scientists from the Departments of Agriculture, Interior, HEW, National Academy of Sciences, observers from the Office of Science and Technology and the Arizona Extension Service concluded the herbicides were not responsible for most injury to plants, any injury to animals, and may have been associated with one minor case of human illness.[6]

Some work has been done attempting to associate DDT residues in females with abnormal births, but no association has been demonstrated.[4]

Mercury is commonly used as a fungicide, besides many other industrial and commercial uses. "The effects on the offspring of mothers ingesting mercury-contaminated fish (disease in Minamata Bay area in 1953 and in Niigata in 1964 in Japan) aroused concern over the teratogenic effects of mercury compounds (82). Severe neurological effects were noted in the children although in many cases the mothers suffered no overt symptoms. The compound responsible was methyl mercury chloride,

which is incorporated into the flesh of the fish through the aquatic food chain beginning with the conversion of metallic mercury on river and lake beds by anaerobic bacteria to alkyl mercury salts."[4]

Summary

In review, "There appears to be no conclusive evidence that the small number of pesticides which have been studied for teratogenic potential actually represent a hazard to humans under normal conditions of pesticide exposure."[4] To ban or restrict the usage of a pesticide that has been shown to be teratogenic to animals."at dose levels which far exceed actual or expected exposures is unreasonable and could well deny usage of chemicals whose benefits far outweigh risks."[5]

It is difficult to extrapolate teratologic findings in animals to man, for man and animals differ in sensitivity to the pesticide. It is also difficult to pinpoint malformations in human fetuses as arising from any specific agent, particularly if a substance is a low-incidence teratogen. There is no good epidemiological evidence implicating pesticides in teratological toxicity in man.[1,4] However, much more research in this area is needed.

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Chronic Biologic Hazards of Pesticides

CARCINOGENESIS

Burton R. Evans

Introduction

Carcinogenesis is the production of malignant new growth made up of epithelial cells that tend to infiltrate the surrounding tissues and organs. A carcinogen is a cancer-producing substance. Viruses and a wide variety of chemical agents have produced cancerous growth in experimental animals. A great deal of this effort has been directed to better understanding the causes of cancerous growth in man and, by this, prevention and treatment. One of the most important cancers concerned with man's health is lung cancer. Carcinoma of the bronchus, or lung cancer, has become the most frequent form of cancer in men in the United States and other countries, and is increasing. In the state of Connecticut the incidence increased from 22/100,000 in males in 1945-1949 to 46/100,000 in 1960-1962. A similar pattern has been shown in other states.[1]

In 1968 about 60,000 Americans developed cancer of the lung. The incidence in males doubled in Denmark between 1943 and 1957. There seems to be no doubt the increase of cancer of the lung is real. While there are many causes of lung cancer, all the evidence suggests these are environmental products of modern civilization.

Associated Carcinogens with Lung Cancer

Cigarette smoking and atmospheric pollution have been suggested as causal factors. The most important cause identified to date has been the inhalation of tobacco smoke. The rate of bronchial carcinoma (lung cancer) in smokers of more than two packages of cigarettes daily was 217/100,000 - a rate sixty times greater than for men who never smoked.[2] At least 21 retrospective and three prospective investigations[3] have been carried out and in every case a correlation between cigarettes smoked and the incidence of lung cancer has been found. While lung cancer has not been reproduced in animals experimentally, it has been so consistently associated with cigarette smoking that most workers accept it as a causal factor. Some workers believe there is a lapse of about twenty years between exposure to a carcinogen, such as cigarette smoke, and the development of cancer.

Atmospheric pollution is higher in urban areas than rural ones. It seems logical that if air pollution plays a part in the development of lung cancer, it should be possible to demonstrate the death rate from cancer of the lung is higher in the towns than in the country. Carcinogenic compounds have been identified in urban air pollution.[6] Mills[7] showed twice the prevailing lung cancer incidence rates in urban residents driving over 12,000 miles per year in urban traffic as opposed to those living in the city not driving this amount. Several other studies support the view that the incidence in the industrial areas is higher than the agricultural areas.[1] For example, a higher occurrence of lung cancer was reported in the bay area of San Francisco, Los Angeles, and San Diego than in the remaining rural areas.[10] These types of studies involving atmospheric pollution are very difficult to do and arrive at convincing data. It must be remembered that, unlike an occupational hazard, atmospheric pollution affects all living in the same locality more or less in the same way, and that it is difficult to adduce convincing evidence for its action.[8]

There have been a large number of chemicals that have been identified as carcinogens in animals; the effect of many of these on man in the dosages he is exposed to are not known for most of them. There are certain occupations that are exposed to large amounts of a particular substance where cancer has been associated. Since the respiratory system becomes heavily involved in any situation where foreign substances are suspended in the air, it is natural to assume that the cancer involved in some occupations would be lung cancer. There is adequate experimental and epidemiological evidence to incriminate various organic and inorganic industry-related chemicals as causes of cancer of the lung. This is supported by experimental investigations in which cancer of the lung has been produced in animals exposed to radioactive metals, nickel, chromium and arsenic.[1] For example, occupational arsenic poisoning has been associated with lung cancer in vine growers in Beaujolais.[5]

It has become apparent that there is a risk of cancer of the lung in persons exposed to asbestos--not only to workers in the asbestos industry, but also those living in the area where the industry is located.[1] Inhalation of asbestos fibers leads to asbestosis, a fibrotic condition of the lung. The first indication of a carcinogenic hazard in asbestos workers came from a study of the association between this condition and lung cancer. Bonser, Faulds, and Steward (1955)[8] for example, in a series of 72 asbestosis victims, found 12 cases of carcinoma of th lung in males. The balance of evidence suggests that asbestosis is frequently associated with lung cancer,and thus that work with asbestos under bad conditions is liable to a higher incidence of lung cancer than normal.

In these types of studies where you are attempting to associate some environmental factor with lung cancer it is necessary to compare two groups of people as nearly alike as possible with only one variable in one group associated with factor "X" and one not associated with it. The trick then is to determine if the one variable (factor "X" such as cigarette smoking or asbestos) is associated with the disease in question. The stronger the association, the greater the evidence that factor "X" is involved. The greatest problem with this type of study is that it is very difficult to be certain only one variable is involved. Differences in age, race, sex, socio-economic status, residence, occupation, and others may be very significant variables in the two populations one is attempting to compare.

Pesticides and Carcinogenesis

There are about 500 pesticides in common use. Many reports have been published to establish or refute a causal relationship of pesticides to cancer. Studies have been along two lines, one: dosing rats with a particular pesticide to determine if tumors result; second, studying human populations--either determining if individuals occupationally working with pesticides have a higher incidence of cancer than those not so exposed, or in determining if a group of people already with cancer have higher levels of pesticide in their tissues than a control group.

Various pesticides representing different classes of pesticides have produced tumors in mice and can be rated as carcinogenic. These include p,p' DDT, Aramite, and Mirex. At this point in time it is not possible to show why certain chemical structures are carcinogenic and others are not. Extrapolation of results from mice to men is always a problem. As far as is known, cancer, due to pesticide exposure in man has not been reported.

Various studies have been done on groups of people occupationally exposed to pesticides, but there is no evidence they were more at risk than the controls. Likewise, several studies have been done on pesticide residue levels from tissues of individuals with cancer, but most of these have failed to show any correlation between pesticide residue levels and cancer.

In a pilot study in California,[12] the cytologic characteristics of sputum were studied from 1362 individuals exposed to pesticides, and 419 controls. Five cytologic characteristics were recorded: Inflammation - number of pus cells; Irritation - increased number of macrophages and/or increased shedding of bronchial mucosal cells; Allergy - increased number of eosinophils; Obstruction - increased fibrin and Curschmann's spirals; and Metaplasia - increased prevalence of cells suggestive of squamous metaplasia of bronchial epithelium.

"In certain other chronic irritations histologic alteration takes place in the mucous membrane of the bronchial tree. This is the squamous metaplasia. In squamous metaplasia, portions of the normal pseudostratified columnar epithelium in the bronchial mucosa are replaced by a stratified squamous epithelium. When this new metaplastic epithelium has the same structure as the natural stratified squamous epithelium, the exfoliated cells are indistinguishable from the normal squamous epithelial cells."[13]

Exposed and controls were compared with these variables with the following results:

Comparison of Sputum Cytology Between a Pesticide Exposed and a Non-Exposed Pesticide Group

Characteristic	Controls (419) Percent Showing	Exposed (1,362) Percent Showing
Inflammation	40%	36%
Irritation	29%	29%
Allergy	9%	8%
Obstruction	12%	9%
Metaplasia	27%	43%

"Of these five characteristics studied, only metaplasia was greater among the exposed than the controls. Detailed analysis of age and smoking habits failed to account for these differences. Comparison with the prevalence of metaplasia in other occupational groups indicate the prevalence of metaplasia in pesticide workers is clearly excessive."[12]

What is the significance of finding a larger number of "metaplastic cells" in the sputum of pesticide exposed individuals? There is no unanimity of opinion among cytologist. "Some state firmly that metaplasia has no connection with the development of lung cancer. Others believe that the transformation of bronchial epithelium to a squamous cell type is an essential first step in the development of squamous carcinoma of the bronchus since 'metaplastic cells' are almost always found in large numbers in sputum smears which also contain malignant squamous cells. It is important to emphasize that essentially all experienced cytologist agree that the converse is not true; namely, the presence of 'metaplastic cells' by no means implies impending malignancy. All agree, also, that metaplasia is a reversible condition."[12] The possible implication of these findings to human health demand further investigation, and this is now in progress.

Summary

A number of products of our modern environment have been associated with cancer, many others have been demonstrated as carcinogenic on animals. Their long-term effect upon man is unknown. A number of pesticides have been demonstrated as

carcinogenic and likewise their long-term effect is not known. The accumulative effect of several carcinogens or synergistic effect of a carcinogen and other chemicals working together is again not known. Due to a wide spread usage and distribution of pesticides in our environment, it is obvious that continued long-term studies will be necessary to monitor the possible hazards of pesticide carcinogens to man's health.

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MAN'S EXPOSURE TO PESTICIDES

Anne R. Yobs, M.D.

Pesticide chemicals are ubiquitous. Their presence has been reported in every part of the environment--air, water, soils, crops, food, feeds, and many species of wildlife--and in some occupational settings. The exact pesticide and its concentration reported in the several parts of the environment vary with time and geographic location of the study as well as with the sampling and analytical techniques used by the investigator. Exposure to pesticide chemicals can and does occur in the urban situation as well as on the farm, although concentrations are generally lower in the city. In today's cosmopolitan culture, certain of these chemicals are used to prevent insect damage to clothing and such household items as carpeting and rugs, to control fleas and other insects on pets, to prevent disease spread through control of insect vectors both over land and in airplanes, and to control insects as well as rodents in the home and garden. Pesticides may also be found in cosmetics which contain lanolin, an oil of animal origin.[1]

Pesticides, like many other materials, may be transported great distances once they have entered the air (and atmosphere) or water. Therefore, it can no longer be assumed that one's exposure will be limited to those chemicals which are used locally.

In order for a chemical substance to affect a living organism, it must come in contact with the organism or actually enter the body--that is be absorbed into it. Humans like other mammals may absorb pesticides through the gastrointestinal tract or by ingestion; through the pulmonary tract or by respiration; and across or through the intact skin; i.e., percutaneous. For most of these chemicals, absorption is most efficient by ingestion. For others, however, absorption is just as efficient--and for some even more efficient--when exposure is primarily through the respiratory tree or the skin.

Many approaches have been used in the past in attempts to determine man's exposure to one or more pesticides. These have included the collection and analysis of individual sample meals or meals for an entire day as was done by Durham and co-workers in 1965.[2] In this study, arrangements were made with participants for two plates to be served at the same time; one was used for chemical analysis while the other was the participant's meal. The Food and Drug Administration's Market Basket Survey takes a somewhat similar approach.[3] Here the diet of a hypothetical 18-year-old man is prepared for the table, then analyzed.

Documentation of respiratory exposure experienced by workers has been attempted by analyzing filter pads from respirators or by measuring the pesticides in air in the region of the worker's nose and mouth using a portable micro-impinger or

other device and subsequently analyzing the collecting media or solvent.[4] Quantitation of percutaneous exposure has been attempted by analysis of cloth patches attached to clothing during exposure and extrapolation of this information to determine what total surface exposure would have been.

In all these, direct measurement of the pollutant itself is attempted under actual exposure conditions. Obviously no one of these approaches measures the total exposure to pesticides from all routes, nor are these approaches practical for application to a number of individuals in an actual situation. Each, however, is a valuable research tool.

Another approach is an indirect one whereby exposure is estimated by quantitating known effects such as modification of enzyme activity. To use this approach, quantifiable effects must be known to result from exposure to a pesticide chemical; ideally these effects should develop in definite increments as the level of exposure increases. Also, the range of activity under normal or unexposed conditions must be relatively narrow and fairly standard with little physiologic variation.

Known pesticide effects on humans are usually similar for an entire group of pesticides, such as liver microsomal induction with chlorinated hydrocarbon exposure, or permanent acetyl cholinesterase inhibition with organophosphates but temporary reversible inhibition of the same enzyme after carbamate exposure, the differences being ones of rate or intensity.

Efforts to identify and document other effects are directed toward study of individuals who have been acutely intoxicated or poisoned by pesticides and other persons who have long-term occupational exposures to pesticides. Both these groups experience pesticide exposure at a level which is many times that of the general population. It is possible that some effects which develop under these circumstances of heavy exposure may also occur at lesser intensity in the general population. The majority of the long-term prospective or epidemiologic studies of the occupationally exposed groups are performed in the Community Studies projects.[5] These studies are established by contract with State Health Departments and/or local medical schools in areas of high or unique pesticide usage. Each project has its own pesticide residue analytical laboratory and usually its own facilities for biochemical testing. Subjects are drawn as volunteers from local groups which are occupationally exposed to pesticides. These may be manufacturers, formulators, professional applicators or farmers; a control group of the general population is also followed by each study. Each volunteer, on entering the study, undergoes a complete physical examination including EKG, hematology, and biochemistry workup as well as appropriate tests for pesticide residue levels--usually in blood--and urinary metabolite excretion. A complete medical and work-exposure history is also taken. These tests and histories are repeated or updated at regular intervals. Data from all projects is then combined for evaluation. From time to time, special efforts are also directed toward study of cellular metaplasia, chromosomal aberration and neurophysiologic changes in these groups. In a nutshell, every effort is made to follow every lead concerning exposure-related health effects and to develop as many leads as possible. The study group is primarily, if not entirely, male. Special studies concern problems of other groups--such as jaundice in the newborn and maternal-fetal pesticide residue levels. Once again, these techniques are valuable in research but are not suitable for routine use in large groups.

How, then, can one determine what is the average man's exposure to pesticides in a practical, fairly routine manner that will permit the development of a mass of valid data over a broad geographic area? The most amenable approach is the measurement of levels of the pesticides and their metabolites which are stored in the body or which are excreted in the urine. Neither of these is appropriate for all pesticides nor even for all groups of pesticides.

The chlorinated hydrocarbon pesticides are relatively stable, are lipotropic and tend to be stored in body fat. Therefore, metabolite levels in adipose reflect the individual's previous exposure to selected ones of the more widely used members of this group--DDT, Dieldrin, the BHC isomers and heptachlor. From these measurements it is possible to estimate previous levels of exposure and to compare exposure between groups. Levels in blood are more affected by recent exposures but levels occur in parts per billion or 10^{-9} grams and consequently fewer pesticides are identifiable.

The presence of DDT in humans was first reported by Laug in 1950[6]. Since that time there have been several reports of studies of pesticide levels in adipose tissue in humans. Usually these have concerned small numbers of individuals in restricted geographic areas.[7] Comparison of results from one investigator with those from other investigators must be done very cautiously because of major changes in analytical technology and because of interlaboratory variation. At such low levels and with instrumental variation, there is ample opportunity for rather wide variation of results. Table 1 summarizes results from these studies.

In 1967, a nationwide program was initiated to measure chlorinated hydrocarbon levels in human adipose of individuals over the country. This Human Monitoring Survey has had a strong interlaboratory quality control program and sampling has been performed according to a statistical design (Table 2). Therefore, it is possible to compare data with some confidence between years, geographic areas, or on age, sex, or racial groupings. It will also be possible to compare data on the basis of diagnoses when sufficient numbers of cases have been collected.

In the occupationally exposed groups, it has for some time been possible to measure urinary excretion of DDA (water soluble metabolite of DDT) or PNP (para-nitrophenol), metabolite of parathion. These tests were not sensitive enough for use with the general population where lower levels of exposure result in metabolite excretion at levels below the sensitivity of the tests. Recent analytical methodology development now makes it possible to estimate exposure to the organophosphate pesticide group by measurement of common metabolites in the urine as well as to other pesticides such as the carbamates, the phenoxy herbicides, etc. through measurement of the parent compound or phenolic metabolites in the urine. These procedures are now being tested in a pilot project to determine their applicability to the general population before adding them to the national program.

You may wonder that I have not included the determination of acetyl cholinesterase activity as a monitoring device in humans. The range of normal for this test is quite broad and is subject to considerable individual variation, a fact which makes this test unsuitable for general population monitoring.

Knowledge about man's exposure to pesticides is important (1) in determining the effects of altered pesticide usage patterns, (2) in determining trends and variations in exposure levels, (3) in fully understanding the impact of pesticides on the ecology and (4) in predicting and studying the incidence of health effects of such exposure(s).

Preliminary evaluation of data from the nationwide survey of chlorinated hydrocarbon levels in humans revealed an unexpected but significant geographic and racial variation in levels of DDT which suggested the existence of another major route of exposure for the general population other than food, most of which in this country is shipped in interstate commerce and so is subject to control of pesticide contamination through a system of legal tolerances. Ambient air was suspected of being this route. There had been little study of pesticide contamination of ambient air. Most work in this field had been problem oriented--that is, study of drift during application or local contamination after application. An energetic program of ambient air sampling over the country has shown considerable geographic and temporal variation of pesticide pollution of air. Such pollution is a potential source of human exposure by respiratory, percutaneous or ingestion and as such would be reflected in the tests which have been discussed.

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TABLE 1

Concentration of DDT-derived Material in Body Fat of the General Population of the U.S.

Year	Location	No. of Samples	Analysis Method	DDT (ppm)	DDE as DDT (ppm)	Total as DDT (ppm)	DDE as DDT (% of total)	Reference
< 1942	Louisville, Ky.	10	Colorimetric	a	a	a	--	Hayes et al., 1958
1950	Washington, D.C.	75	Colorimetric	5.3	--	5.3	--	Laug et al., 1951
1955	Tallahassee, Fla.	49	Colorimetric	7.4	12.5	19.9	63	Hayes et al., 1956
1954-56	Savannah, Ga. and Wenatchee, Wash.	61	Colorimetric	4.9	6.8	11.7	58	Hayes et al., 1958
1956	Atlanta, Ga.	36	Colorimetric	5.5	10.1	15.6	65	Hayes et al, 1971
1961-62	Atlanta, Ga., Louisville, Ky., Phoenix, Ariz., and Wenatchee, Wash.	130	Colorimetric	4.0	8.7	12.7	69	Quinby et al., 1965
1961-62	Wenatchee, Wash.	28[b]	GLC[c]	2.4	4.3	6.7	64	Dale & Quinby, 1963
1962-63	Chicago, Ill.	282	GLC	2.9	8.2	11.1	74	Hoffman et al.,1964
1964	Northeast, Midwest, Deep South, and Far West	64	GLC	2.5	5.1	7.6	67	Zavon et al., 1965
1964	New Orleans, La.	25	GLC	2.3	8.0	10.3	77	Hayes et al., 1965
1962-66	Chicago, Ill.	994	GLC	2.6	7.8	10.4	75	Hoffman et al.,1967
1964-65	Ohio	18	GLC			9.0		Schafer and Campbell, 1966
1964-65	Florida	42	GLC	3.1	7.5	10.6	71	Radomski et al,1968
1964-65	Florida	12	GLC	3.79	7.7	11.5	70	Davies et al.,1965
1965-67	Florida Age Race							
	0-5 W	17	GLC		3.1	5.5	56	Davies et al.,1968
	6+ W	90	GLC		6.1	8.4	73	
	0-5 NW	17	GLC		4.6	7.8	59	
	6+ NW	35	GLC		12.0	16.7	72	
> 1967	Florida	42	GLC	3.13	7.43	10.56	70	Fiserova-Bergerova et al., 1967
1966-67	Hawaii	30[d]	GLC	1.34	5.17	6.51	79	Casarett et al.,1968
		29[e]	GLC	1.40	4.90	6.30	78	
		30[f]	GLC	1.18	4.99	6.17	81	
1966-67	Louisiana	62	GLC TLC	1.32	6.33	7.65	83	Selby et al., 1968
1967	California	64	GLC	4.8	17.9	22.7	79	Rappolt, 1970 Rappolt and Hale, 1968
> 1968	Florida		GLC	Study not yet published in full				Barquet et al.,1970
1967-68	Arizona	70	GLC	1.54	5.10	6.64	77	Morgan and Roan, 1970

[a] Not detected.
[b] These 28 samples were also tested for DDT and DDE content by a colorimetric method. These results are included in the 130 samples listed above.
[c] Gas-liquid chromatography.
[d] Perirenal fat.
[e] mesenteric fat.
[f] panniculus fat.

Table 2

Mean Levels of Selected Chlorinated Hydrocarbon Pesticide Residues in Adipose of the General Population (ppm)

National Summary Data by Year

Human Monitoring Survey

Preliminary Data

Cal year	1967	1968	1968	1969	1970[1]	1971
# samples	722	3300	3237	3264	2626	
# states	11	21	23	33 + DC	27 + DC	
Method	non-cleanup	non-cleanup	Mod. MOG	Mod. MOG	Mod. MOG	Mod. MOG
pp DDT	1.28	1.52	1.53	1.20	1.15	
op DDT	0.06	0.09	0.15	0.13	0.14	
pp DDD	0.13	0.10	0.04	0.04	0.03	
op DDD	0.00	0.00	0.00	0.00	0.00	
pp DDE	4.22	5.28	4.08	4.02	4.12	
op DDE	0.04	0.01	0.04	0.04	0.04	
Total DDT equiv	6.22	7.60	6.26	5.81	5.97	
Heptachlor Epoxide	0.05	0.04	0.06	0.08	0.08	
Dieldrin	0.14	0.12	0.13	0.13	0.15	
α - BHC	0.00	0.00	0.00	0.00	0.00	
β - BHC	0.28	0.28	0.28	0.28	0.29	
Δ - BHC	0.00	0.00	0.00	0.00	0.00	
δ - BHC	0.01	0.00	0.00	0.00	0.00	

[1] Incomplete data 6/6/71

PESTICIDE POISONING—A MEDICAL EXAMINER'S VIEW

B.D. Blackbourne

THE COMMUNITY STUDIED

The occupational and community hazards of a potentially lethal agent may be evaluated by studying clinical and fatal cases of poisoning in a community that has been at risk for a period of time. In Dade County, Florida (Metropolitan Miami), a high utilization level of pesticides has existed over many years. Since the origin of the Medical Examiner's Office in 1956, a high percentage of all fatal poisonings have been documented.

In a subtropical area involved to this extent in agriculture, pesticides are very necessary; but, at the same time, potentially dangerous. An estimated 250,000 pounds of organophosphate pesticides are used annually in Dade County.

During the past twelve years, over 100 persons in Dade County have died as the result of pesticide poisoning (Table 1). Over half of these have been suicidal ingestions. Forty-one accidental fatal poisonings have occurred from organophosphate and non-organophosphate pesticides (Table 2). The peak incidence of fatal accidental poisoning occurred in 1963. Through an educational campaign directed toward agricultural users and the community, the number of deaths has decreased in subsequent years (Table 3).

FATAL ORGANOPHOSPHATE POISONINGS

In 1959, the first Dade County death from organophosphate pesticides (parathion) was recognized. In the ensuing ten years, 56 deaths have resulted from these agents. Of these, 28 were accidental poisonings, 26 suicides, and 2 murders.

Eighteen children died from organophosphate poisoning. Each death represented a separate poisoning incident. In several cases, more than one child ingested the poison. But in each case, only one died. Thirteen of the 18 children poisoned were 2 years of age or younger; the youngest was 14 months old; 15 were Negro, 3 were white; 14 were boys, 4 were girls.

Eight of these 18 children found a bag or bottle of concentrated parathion and ate it. Nine other children ingested small amounts of parathion spread about the house, and especially the kitchen, for control of roaches or rodents. One child died of Guthion poisoning.

The disposal of empty metal cans and drums containing any potent pesticides is a very serious problem. Hot water or caustic washing is not sufficient to rid the container of the pesticide. Complete burning of the inner liner and all of the pesticide residue is the only way that these containers may be reused. For routine disposal, cans should be crushed or otherwise damaged (so that they will serve no secondary purpose) and then buried in the ground.

Accidental occupational organophosphate poisoning resulted in three deaths during this study. Two had sprayed with parathion the day prior to becoming ill. The third man had dusted collard greens all day using a rag over his mouth instead of a respirator.

Organophosphate poisoning associated with acute alcoholism resulted in the death of five men. In each case, while highly intoxicated with ethyl alcohol (0.15-, 0.23-, 0.27-, and 0.44- percent ethanol), they picked up a bottle and, expecting that it was more alcohol, drank it.

As with any potent drug or chemical when it becomes available in the community and its lethal poison potential becomes known, those people intent on suicide will use it. Forty-five percent of the organophosphate deaths have been suicidal poisonings.

Two persons with mischief on their minds turned to parathion. One woman put one drop in the beer glass of a loan shark who was extracting $20 a week from her as interest on a $100 loan. When he rapidly died, she pleaded that she had not intended to kill him--only to make him sick. The other case concerned a man who put parathion in his wife's Kool Aid. Admitted to the hospital in such extreme distress that she could not talk, she wrote "poison" and her common-law husband's name on a pad of paper held by a nurse.

NONFATAL ORGANOPHOSPHATE POISONINGS

An estimated 2,000 nonfatal organophosphate poisonings occur yearly in the United States. This figure may be compared with an estimated 200 fatal poisonings. The majority of both fatal and nonfatal organophosphate poisonings occur in Texas and Florida, where large amounts of these materials are used in agriculture. As in all other forms of poisoning, in order to make a correct diagnosis, someone must suspect a toxic agent as the cause. After reviewing the patient's symptoms, the circumstances of his becoming ill, his age and occupation, and available knowledge about the community, the most-likely responsible agents can be selected and laboratory tests performed. Only through rapid and close communication between those having knowledge of the patient and of the circumstances, the physicians treating the patient, and the chemist performing the tests can the correct poison be identified and therapy initiated.

Briefly, the signs and symptoms of organophosphate poisoning are: increased sweating, increased salivation, muscle jerking, constricted pupils, wheezing, severe abdominal cramps, muscle weakness progressing to paralysis, vomiting and diarrhea, cyanosis and convulsions. Of equal importance in suspecting the diagnosis of organophosphate poisoning is the rapid onset and progression of this unusual symptom complex. If pesticide poisoning is not thought of, the illness may be regarded as a primary lung, brain, or heart disease.

NONFATAL PESTICIDE POISONINGS IN DADE COUNTY, 1964-1968

Ninety-two nonfatal poisonings were documented, 79 of them accidental exposures, 11 attempted suicides, and 2 possible attempted murders. Of the accidental poisonings, 26 resulted from occupational exposure and 41 involved children who had ingested or otherwise had been exposed to the pesticide. Of the 79 accidental poisonings, 40 involved parathion, 12 phosdrin, and 5 diazinon.

FATAL, ACCIDENTAL NONORGANOPHOSPHATE PESTICIDE POISONING

After excluding many suicidal poisonings by nonorganophosphate pesticides, 13 cases of fatal accidental poisoning remain in the Dade County files between 1956 and 1969. The pesticides involved include: those used in building fumigation (4), arsenic (2), tallium (2), phosphorus (3), and paraquat (1).

The first documented fumigation death occurred in 1957--a 27-year old woman. In January, 1963, a home fumigation using acrylonitrile (34 percent) and carbontetrachloride (66 percent) eventually lead to the death of a 41-year-old woman. In December, 1965, a similar situation resulted in the death of a 22-month-old boy. A fourth death related to tent fumigation. A 57-year-old woman alcoholic recently discharged from jail was advised of the plans to fumigate, and said she would pick up her sweater and leave. When the fumigation was completed the following day and the house inspected, the body of the woman was found in the bathroom. Apparently, she had re-entered the house sometime during the night for the purpose of suicide.

Two accidental arsenic deaths have involved small children. The mother of a two-year-old child mixed up some arsenic and water one evening and absentmindedly left it on the kitchen table. The youngster arose before her mother the next morning and drank the liquid, thinking it was water. She lived 24 hours in the hospital. The other child, 17 months old, apparently found a container of arsenic because white powder was noted on his face when he became dizzy and began to cry. He died 2 hours later.

The two recorded victims of thallium poisoning were 3 and 16 years of age, respectively. Their uncle found a gallon jug of light yellow liquid in a ditch beside the road. Thinking that it was motor oil, he took it home. The father of the two victims tasted it and recognized it as honey. If the container had ever been labelled, the label had come off, for there was no warning on the glass jug of the powerful poison it contained. The 16-year-old died 16 days after ingesting the honey, his 3-year-old sister died 4 weeks after eating the same honey. The other members of the family survived.

The three phosphorus deaths include two children and an intoxicated man, who had all ingested phosphorus. They each died from 3 to 9 hours after ingesting the poison.

The single accidental paraquat poisoning involved an alcoholic woman who, while intoxicated, drank a solution of paraquat thinking it was more liquor. Her husband had brought the paraquat home for use in the yard.

WHAT CAN BE DONE

Action to reduce the fatalities and clinical poisonings from pesticides must involve education of the agricultural handlers of pesticides, and also of the general public.

Safety equipment--including gloves, face masks, and protective clothing--have been prescribed for loaders, spraymen, flagmen, and others. This equipment must, however, be used to be effective.

Pesticide container disposal is a problem. Washing with hot water and soap will not remove all of the pesticide residue; the potential for poisoning remains. Large drums may be commercially reconditioned by burning the inner liner. Smaller containers should be crushed or split with an axe so they will serve no secondary purpose and then buried in the ground.

Pesticides are poisons and must be labelled. If removed from the original labelled container, subsequent containers must indicate by prominent label description the nature of the contents. All labels must be so affixed to the container that they will not be rubbed off or washed off by rain. Potent and highly toxic agricultural pesticides have no place in the home. Under no circumstances should pesticides be placed in food containers. No bait made by placing a pesticide on food is acceptable for home use.

SUMMARY

During a twelve-year period in Dade County, Florida, 41 deaths occurred from accidental pesticide poisoning. Twenty-five children were poisoned. Seven poisonings occurred during commercial use of pesticide and 7 involved persons who drank the pesticide while acutely intoxicated on ethyl alcohol.

Five principles are suggested to reduce fatal and clinical poisoning:

1. Observe precautions prescribed for the safe handling of pesticides in agriculture.

2. Make sure that pesticide containers are safely disposed of.

3. Do not take agricultural pesticide home for storage, or for use against household pests.

4. Do not place pesticides on food as bait or in food containers for storage or transportation.

5. Always label pesticide containers so that the label cannot be washed off or rubbed off.

Table 1. Pesticide Poisonings, Dade County, Florida, 1956-1968

	Organo-phosphate	Nonorgano-phosphate	Sub total	Total
ACCIDENTAL	28	13	25	41
Children	18	7	7	
Occupational	3	4	7	
Alcohol	5	2	2	
Miscellaneous	2			
SUICIDE	26	46		72
HOMICIDE	2	2		4
TOTAL	56	61		117

Table 2. Pesticides Causing Accidental Death

Pesticide	Number of deaths
Parathion	26
Guthion	1
V.C. 13	1
Methyl bromide	1
Acrylonitrile	3
Arsenic	2
Thallium	2
Phosphorus	3
Paraquat	1
Real Kill	1
TOTAL	41

Table 3. Accidental Pesticide Poisoning, Yearly Incidence, 1957-1968

Year	Fatal	Nonfatal
1957	1	NA
1958	7	NA
1959	5	NA
1960	2	NA
1961	2	NA
1962	1	NA
1963	9	NA
1964	4	22
1965	3	24
1966	2	11
1967	2	11
1968	3	11
TOTAL	41	79

NA--Information not available

Table 4. Nonfatal Pesticide Poisoning, 1964-1968, Dade County, Florida

Accidental poisoning	79
Children	41
Occupational	26
Miscellaneous	12
Attempted suicide	11
Attempted murder	2
TOTAL	92

Table 5. Nonfatal Accidental Pesticide Poisoning, 1964-1968

Poisoning					Pesticide							
Year	Children	Occupational	Other	Total Accidental Poisonings	Parathion	Phosdrin	Diazinon	Thallium	Phosphorus	Arsenic	Mercury	Other
1964	13	5	4	22	9	1	4	1	2	1		4
1965	10	12	2	24	14	7						3
1966	5	4	2	11	7	3						1
1967	6	4	1	11	5	1				1	2	2
1968	7	1	3	11	5		1				1	4
TOTAL	41	26	12	79	40	12	5	1	2	2	3	14

Table 6. Fatal Accidental Pesticide Poisoning, 1964-1968

Poisoning					Pesticide			
Year	Children	Occupational	Other	Total Accidental Poisonings	Parathion	Guthion	Acrylonitrile	Paraquat
1964	3		1	4	3	1		
1965	3			3	2		1	
1966	1		1	2	2			
1967			2	2	2			
1968	1		2	3	2			1
TOTAL	8	0	6	14	11	1	1	1

POISON CONTROL CENTERS AND THEIR FUNCTIONS

Henry L. Verhulst

Following World War II, there was a proliferation of new chemicals and new common household products. The names, characteristics, and toxicity of these new chemicals were unfamiliar to practicing physicians. Even the medicines which were their tools had unknown facets when they were ingested in an acute overdose. Manufacturers who might expound on their drugs' therapeutic effects, or reveal their collection of reported adverse reactions, frequently had few data on acute overdosage. These were new problems to the physicians. However, many of the old problems never had been resolved completely, and if they had, this information had not received wide circulation. Among the latter were such questions as: were matches really poisonous; did shoe dyes actually contain aniline and, if so, which ones; and why tobacco with its high nicotine content was not causing fatalities among children who were ingesting it.

According to a 1950 survey, over 50 percent of children's accidents reported to pediatricians were due to potential poison ingestions. At the same time, the pediatrician was understandably unfamiliar with such chemicals as sodium tripolyphosphate, ammonium thioglycollate, dimethyldistearyl ammonium chloride, and many other chemical ingredients found in household products. However, knowledge of these chemicals was necessary for the proper treatment of an ingestion.

Because of this knowledge gap and because there were hundreds of thousands of such ingestions annually, the Illinois Chapter of the American Academy of Pediatrics initiated a pilot project in Chicago known as the "POISON CONTROL CENTER." From its inception the project received the cooperation of the pediatric services in the local major hospitals, the State Health Department, and the State Toxicological Laboratory. With these organizations serving as a catalyst, a working unit was formed representing the local medical society, some 20 hospitals, four full-time health departments, five medical colleges, the Illinois Chapter of the Academy of Pediatrics, and the American Public Health Association.

The Chicago Poison Control Center opened in November 1953. It provided information on and treatment for poisonings, and had the further objective of establishing a program of prevention. The number of other poison control groups which subsequently were organized with the same goals as those of the Chicago Center can be considered a tribute to the latter's success. The new centers soon found, however, that they were duplicating one another's work in compiling information and that some information gathered by one center was not always being distributed to the others. Moreover, clinical and epidemiological information about poisoning experiences were not being collected. It became apparent that some coordination of poison control center activities was necessary.

By 1956, sixteen (16) centers had been established in major metropolitan areas. Most were established by the pediatric service of the childrens centers in the area. New York City's, the only exception, was placed in the Health Department. The operation of all the centers was fairly uniform. The chief of the pediatric service served as the director. Residents staffed the program and answered requests for information. The hospital assisted in purchasing necessary texts, journals, and special reference material. Descriptions of the first centers made it clear that the program was utilized mainly by physicians treating emergency ingestions.

The poison control movement gained much publicity and resultant popularity throughout the nation. Because of this, many civic organizations as well as medical and paramedical organizations encouraged establishment of poison control centers in local hospitals. Unfortunately, in some instances, the local hospital had insufficient personnel to perform the functions. The community might have had better service had they concentrated on improving the emergency treatment facilities and utilized a center in one of the larger medical centers for information services.

We have continued to stress the need to differentiate between Poison Control Centers and Treatment Centers. The designation of poison control centers is made by State Health Departments since medical practice is licensed by the State. However, the individual States have interpreted the guidelines for centers differently. Thus, we have one center in Oregon located at the medical school compared to approximately 100 in the State of Illinois, but, most States have less than twenty (20) centers. The expertise of the staffs of the poison control centers appears to us, and other knowledgeable observers, to increase with the number of calls received. It seems, therefore, that the limited number of centers, designated by most states, would have advantages. We now have a total of 560 designated centers.

The impact of the program to a hospital serving as a center is illustrated by an article on the Boston Center.* It states the number of calls increased from an average of 20 per month in 1954 to nearly 500 per month in 1960. Seventy (70) percent of the calls were from the public. The report also gives information on seriousness of ingestion of 800 cases. Thirty-six (36) percent required no treatment, twenty-nine (29) percent received home treatment, thirty-one (31) percent were treated at the hospital and four (4) percent did not give the information.

The function of the poison control center, then, is to have available information on the formulation of household products or chemicals so information on the toxicity, symptomatology and treatment may be furnished when an emergency occurs. This is not nearly as simple as it might sound. With the exception of medications and a few chemicals which have been ingested frequently, there is limited data except that obtained from animal studies. In many cases no animal data is available on combinations of chemicals, but only the individual components. In such cases only individual data can be given and it is necessary that the physician, or the center, determine the possible extent of the danger. There are some who believe such estimations are subject to many errors. This may be true, but, some action must be taken. Here, the busy center has the advantage since the chance of a previous experience is greater and it can call on past knowledge.

Some of you who have utilized a center are probably concerned by the general nature of the treatment given. There is a mistaken impression that a specific antidote exists for every poisoning. This is not true. In reality, only six or seven specific antidotes are available. Several of these are effective for more than one chemical, but, still the number of substances so treated is small. The rest of the information involves symptomatic treatment and contraindications which may be life saving.

I believe it is necessary that we discuss several areas in which poison control centers are of very limited value. First, they are not laboratories to perform chemical analysis on unknown products or gastric contents. The public has an impression that modern science has progressed to a point that the identification of an unknown substance is but a few minutes work. Most of you know this is not correct. It can require many hours or days of experts' time with the most expensive equipment to identify some unknowns. Second, center personnel cannot make a diagnosis that a patient's clinical condition is necessarily associated to a chemical exposure. They can only give the signs and symptoms of a chemical intoxication. The treating physician must decide if the illness is related to the exposure.

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*Robb, Elwood and Haggerty, Evaluation of a Poison Control Center-American Journal of Public Health 53:1751 (November 1963)

Now I should like to discuss the historical evolution of the National Clearinghouse. --

On November 12, 1956, at a meeting of The American Public Health Association, a recommendation was made that a National Clearinghouse for Poison Control Centers be set up by the U. S. Department of Health, Education, and Welfare. This meeting was attended by representatives from poison control centers and from such national organizations and government agencies as the American Academy of Pediatrics, The American Pharmaceutical Association, the Food and Drug Administration, the National Research Council, the Children's Bureau of the Public Health Service. In compliance with the recommendation, the National Clearinghouse for Poison Control Centers was designated as an activity of the Public Health Service in the Accident Prevention Program. It is now located in the Food and Drug Administration, Office of Product Safety.

The National Clearinghouse contacts industry for the information that manufacturers and distributors can contribute on their products. In this way, it is possible to keep track of new products which may be poisonous and of changes in the composition of existing products. Government agencies are also a source of a large amount of significant data.

There is increasing willingness by industry to supply information about their products, although the material submitted varies greatly. In some cases we are supplied only formulations. Some furnish expected symptoms and/or treatment recommendations. Fewer supply information on toxicity. However, there has been a noticeable increase in information supplied since the passage of the Federal Substances Labeling Act of 1960. Most manufacturers now determine if the LD_{50} is less or greater than 5 gm/kg., which is the limit set by that Act. Once information on the formulation is obtained, a statement of toxicity and treatment is developed by the Clearinghouse, if one is not included by the Company.

An indexed card file for use of all poison control centers has been distributed. The cards in this file are indexed by trade name and contain such information as composition, concentration, and lethal dose of each specific agent; plus symptoms and treatment of poisoning by the agent. Supplements are sent to the centers as new products come on the market, and as existing products come to the attention of the Clearinghouse. A more extensive card file system is kept at the National Clearinghouse.

A bulletin is published periodically containing trends and statistics obtained from the poison report form analysis. New work done on poisonous or potentially poisonous materials, reports of new treatments for poisonings found in the literature or used by individual poison control centers, interesting cases of poisoning and abstracts from the literature on poisoning are contained in the periodic bulletins.

The Division of Poison Control has developed a reporting system through poison control centers to maintain surveillance of products being ingested, inhaled or absorbed to determine any hazards produced, extent of damage and treatment rendered. The system could better be called a monitoring program since we receive reports only when information is sought from a center by a parent or physician following an exposure. Many cases are treated by hospitals and physicians who already have sufficient toxicity information. Also, we get only limited fatality reports since death may occur days after the ingestion and a follow-up report is not always made. Nevertheless, with 115,000 reports received in 1970 we believe we have a representative cross section of products which are taken by children and

those which are causing injury. Semi-annual tabulations are run for internal use by the Food and Drug Administration. Copies are available to the Department of Agriculture. Individual experience with products is supplied to the manufacturer of the product on request. This system does not provide data about environmental contamination or the possible long-term hazard of a chemical. Within the last three or four years there has been, however, a great increase in reports of intentional ingestions. The number of calls requesting treatment information for intentional ingestions has risen steadily to a point where one center reported 50 percent involvement.

Discussion:

Data collected for many years demonstrate that children under 5 years are still the primary group involved in accidental poisoning. The 1970 poison control centers reported 76,155 ingestions to us for this age group. Medicines represented about 50 percent of the ingestions. Of interest to us is the 30 percent reduction in aspirin ingestion in the past two years. Much time and effort have been spent in programs to educate parents that this product should be stored out of reach of children. This reduction is an indication that such efforts can be fruitful over extended periods of time.

Cleaning and polishing agents represent 14.4 percent of the reported ingestions. The most serious categories in this group are the caustics and petroleum distillated contained in furniture polish. The hospitalization rates are approximately 20 per cent and 11 percent respectively. Pesticides account for 5.2 percent. Insecticides and rodenticides are most frequently involved. Hospitalization is reported at 6 percent level. For reference, 5 percent of all children are reported to be hospitalized although some for overnight observation. A table reporting data by category of products is included for your review.

The program has given us information on some real problem areas and removed pressure on others. With a few exceptions, cosmetics have not created a problem. Caustics are still a threat to the health of any child obtaining them, as are some products containing petroleum distillates, particularly mineral seal oil. Carbon Tetrachloride is now banned as a household product. However, there is an allowance for small amounts left as residual during manufacturing processes. Data collected through the reporting system has supported several actions to ban other products which are dangerous for consumer use.

Recent legislation can require changes in formulation of some common household products. It will be necessary that careful evaluation of all substitute chemicals be made to determine their safety as well as the overall product safety. However, there must continue to be a constant surveillance of data from human experience, for animal studies are not always indicative of human reaction to a chemical. We believe the data collection system through poison control centers will enable us to maintain this surveillance.

For several years we have been developing and testing a system for computer retrieval and delivery of the information to centers. This will eliminate lost cards and expedite adding information. Centers in Boston, New Orleans, Detroit, and Kansas City are using a program with approximately 5,000 items on the data bank as a pilot program. Accumulation of data concerning injuries is necessary for proper evaluation of hazard and treatment recommendations. This has been expedited through use of automated data processing equipment. Statistical data from poison reports have been so tabulated by trade name for the past two years. The data in the bank will also include a statement of results of previous ingestions as reported through the centers. Thus, the physician will be aware of injuries caused by a product during the previous year. Information is delivered by telephone lines and displayed on Cathode ray tubes. We are very pleased with the results.

PESTICIDES IN AN OCCUPATIONAL SETTING

Louis Kaplan

The New Jersey Pesticide Project has a unique opportunity to study workers in the pesticide industry, since the State has the largest concentration of pesticide plants in the country. Because we do have so many plants, much of the information and data for this report comes from our experience and work in New Jersey. It should be noted that there is really very little difference between a plant in New Jersey and one in Colorado, Florida, or any other state. The observations and conclusions herein included generally apply equally, I would think, to the workers in most pesticide plants.

Our state has approximately 140 pesticide formulating, manufacturing, and distributing plants, employing about 5000 plus pesticide-exposed workers. Most of the material in this presentation is derived from continuing studies of 132 pesticide workers in nine plants and a concentrated study of a herbicide plant of 73 employees. Thus, a total of 205 pesticide workers is involved.

Long-term participants in the program have been given regular physical examinations, electrocardiograms, chest x-rays, and a complete spectrum of biochemical examinations. Results are compared with a control group of 52 minimally exposed subjects. In addition, our field men are routinely in contact with the participants to keep their occupational and medical histories current.

Some general characteristics of most pesticide plants are: few employees (usually 20 or less), makeshift equipment and plant, minimal supervision, poorly designed exhaust ventilation, and insufficient and rarely used personal protective equipment and sanitation facilities.

Some, not all, plants of large national concerns present a different picture. Usually, they employ more than 20 workers, are well supervised, supply uniforms and good personal protective equipment, occupy well designed quarters, and have adequate equipment for manufacturing, processing, ventilation, and prevention of environmental contamination problems.

Pesticide Plants in the Program

Perhaps a profile of a typical pesticide formulating plant would be helpful at this time.

Plant A - Profile of a Typical Pesticide Formulating Plant

Formulating Plant "A," located near Trenton, is engaged in the custom formulation of pesticide chemicals. Customers include many other New Jersey pesticide companies, Central Jersey farmers, custom pesticide applicators and pest control operators. This plant formulates a

variety of pesticide chemicals, the bulk of which consists of organic phosphates and chlorinated hydrocarbons. A partial list of finished products includes: Parathion, Guthion, Malathion, Abate, Baytex, DDT, Aldrin, Chlordane, Lindane, Dieldrin, and Sevin. This plant employs a total of 22; 19 male workers being directly engaged in pesticide handling activities. Employment is quite stable, with low turnover. Specific operations include: milling and mixing of wettable powders and dusts, granule impregnation, liquid mixing, packaging, warehousing, and shipping. Operations are to a large extent manual. There are small batch operations, and larger production runs of single pesticides, such as Malathion.

The following protective equipment is supplied but its use is more or less left to the discretion of the individual (this means almost never used): approved respirators, nuisance dust respirators, rubber gloves, rubber aprons, face shields, and some hats. Fairly effective local exhaust ventilation is provided at the dust mill (feed site and discharge site of mixed pesticide dust) and the granular mill (bagging site). Design of hoods of these exhaust systems is poor and airborne contaminants can be observed in the plant environment. No local exhaust ventilation is provided for the liquid mixing operation, which is in the same building with the above-mentioned milling operations, located near a pyrethrin-blending operation in an adjacent building. Most workers spend the majority of their time within the main building, and are exposed to pesticides, both at their particular duty station and contamination from adjacent operations. Plant housekeeping is a continuing problem, as the building is not particularly designed to facilitate clean-up. The bulk contamination of floors is usually removed by manual sweeping methods on a daily basis, hopefully; usually toward the end of a work shift, which results in further contamination and exposure hazard. From time to time, when working with chlorinated hydrocarbons, the mixing operator has been observed preparing laboratory control samples with his bare hands. Workers in this plant, besides never showering at work, generally, do not remove their work clothes or work shoes when leaving the plant. They go home as they are, and of course take all the goodies with them, to be distributed to the whole family. The best you can say about their protective and hygienic precautions is that they occasionally wash their hands. A number of acute pesticide intoxications have occurred here, and subacute incidents are commonplace.

A few brief comments on some of the other plants are in order. One large plant provides dust milling by air-impaction methods, blending and packaging services. Although it formulates a number of compounds, the main pesticide formulated there is Carbaryl. This plant produced considerable amounts of DDT up until 1963, and serum residues of DDT and DDE are consistently high in those senior employees who formerly worked on DDT.

An interesting case came to light in this plant. One worker showed zero DDT and DDE residues in his blood. After an investigation and many evasions, this man finally admitted that he was on an anticonvulsant regimen for epilepsy.

Another plant is a general formulating plant, with intensive operations in liquid, granular, and dust formulating of organophosphates. Much parathion work is done here. Although this is what we would call a "clean" plant, the employees are sufficiently exposed to the more toxic organophosphates to cause frequent cholinesterase depressions and complaints of dizziness, nausea, weakness, etc.

Other plants monitored are general formulating plants, where the workers are exposed to a variety of pesticides, and where plant health and safety conditions are uniformly poor.

Environmental Sampling in Plant A

Table 1 shows a comparison of environmental air samples taken in a plant which does a considerable amount of organochlorine formulating; as opposed to results obtained in random outdoor sampling. Note the comparatively large amounts of DDT, DDE, and DDD in the air of the pesticide plant. Also, please note that the plant residues are in mgm per cubic meter, and the outside residues are in nanograms per cubic meter. Converting, we get 570,000 to 7,200,000 ng/M^3 of DDT in the plant, compared to 0.6-3.2 ng/M^3 in the outside ambient air.

TABLE 1

Comparison of Environmental Air Sampling*
(Range)

	p,p'-DDT	p,p'-DDE	p,p'-DDD
Plant A (mg/M^3)	0.57-7.2	0.018-0.20	0.027-0.43
Ambient Air (ng/M^3)	0.6-3.2	0-1.0	0-T

*In-plant sampling vs. random outdoor sampling.

Pesticide Industry Fires

We have experienced three pesticide industry fires over the past few years, and we would like to briefly discuss one which was considered a major conflagration. In August 1971, a multi-building chemical warehouse in Kearny, New Jersey was destroyed by fire. Products included: Vapona, Gardona, Phosdrin, Ciodrin, Aldrin, Dieldrin, Endrin, and many others. There was at least a 12-hour lag before the parent company and the State authorities were notified. Suffice it to say, that proper procedures in fighting this fire were, generally, not observed. Disposal of the pesticide resides and debris was the subject of numerous conferences and meetings. Finally, a plan emerged to place the debris in segregated, above-ground concrete basins, separating the organochlorines from the organophosphates, and treating with lime to maintain an alkaline pH. The organophosphates were to be treated until decomposed; and, the organochlorines were to be monitored regularly, and finally disposed of by methods stipulated by the State, such as incineration at high temperatures (900-1,000° C) in an adequate facility, equipped with an efficient collection system for removal of toxic dusts and gases. A recent check-up on the disposal sites revealed a great many inadequacies in carrying out the disposal plans. The concrete basins were not completed, pesticides were haphazardly dumped on the ground, etc. It is quite apparent that proper guidelines must be established in handling pesticide fires, and proper control, inspection and follow-up procedures worked out by the State Department of Environmental Protection. From our experiences, industry's Pesticide Safety Team Network did not work, and it is strongly suggested that the proper State authorities, with the cooperation of the Federal Environmental Protection Agency handle such emergencies rather than rely on the Pesticide Safety Team Network to do so.

Reports on Studies Made in New Jersey

Appreciable differences in blood cholinesterase serum pesticide residues, urinary metabolites, and biological testing continue to be observed in our pesticide-exposed group, as compared to the controls. Periodic highly elevated DDT and DDE blood residues are being found in ex-DDT formulators. The highest value of 700 parts per billion was found in a service worker, who has not formulated since 1958. Incidentally, this worker recently died of a heart attack. Imagine what our esteemed biostatisticians could do with this piece of information--such as predicting heart attacks based on sera DDT residues, using the Weibull mortality function.

We continue to see a number of sub-clinical and clinical pesticide poisoning cases among our subjects, especially when exposed to the more toxic organophosphates, such as parathion and phosdrin. In these plants, where toxic organophosphates are formulated, abnormal cholinesterase values were and are commonplace. Twenty-eight out of 110 cases of pesticide poisonings investigated by the Project are pesticide workers.

Table 2 demonstrates percent abnormals in cholinesterase and pesticide residues.

TABLE 2

Abnormal Cholinesterase and Pesticide Residues in Industrial Workers

	Cholinesterase (I.U.)			Serum Residues (ppb)		
	No.	RBC (< 8)	Plasma (<3)	DDT (>20)	DDE (>30)	Dieldrin (> 5)
Industry	132	15%	24%	45%	61%	38%
Controls	64	8%	11%	0%	14%	0%

Table 3 compares serum pesticide residues of formulators, general population, and controls.

TABLE 3

Comparison - Serum Pesticide Residues (ppb)

	Controls		General Population		Formulators	
Residue	Mean	Range	Mean	Range	Mean	Range
p,p'-DDT	4.4	0-23	5.6	1-12	28.9	0-304
p,p'-DDE	14.3	0-27	20.8	7-67	28.0	2-187
Dieldrin	1.1	0- 6	1.3	0- 5	7.5	0- 64
Sample Size	54		57		65	

Table 4 reports the percentage of tests which were outside the normal ranges for the blood biochemistries. Some biochemical responses showing differences from the controls were: glucose, uric acid, cholesterol, calcium, lactic dehydrogenase, alkaline phosphatase, transaminases (SGOT and SGPT), creatine phosphokinase, creatinine, albumin.

TABLE 4

Biochemistry (SMA-12)
(Values cited are percentages of total tests showing abnormal results)

	Controls (N = 112)	Industry (N = 150)
Glucose	9.8	16.7
Uric Acid	3.6	7.3
Cholesterol	17.0	24.3
Calcium	3.6	9.4
LDH	16.1	24.7
Alkaline Phosphatase	8.1	17.7
SGOT	13.4	16.0
SGPT	4.5	8.0
CPK	6.2	9.3
Creatinine	0.9	5.4
Albumin	8.9	14.7

In a morbidity study, a review was made of all the positive and abnormal physical findings of our control group versus our pesticide industry group. These data were obtained by medical examinations and medical histories.

In Table 5, significant differences are noted in chronic cough and sinusitis, dizziness and headache, hearing difficulties, and hypertension. Positive nervous system findings occur in 50 percent of the pesticide industry workers as compared to 35 percent of the controls. Gastrointestinal complaints were 7.5 percent in controls and 12 percent in industry. Back problems are twice as prevalent in the industry group.

TABLE 5

Number of Positive Physical Findings
Pesticide Industry vs. Controls

Category	Controls (40)	Pesticide Industry (112)
Back Trouble	5	24
Chronic Cough and Sinusitis	6	31
Dizziness and Headache	3	18
Hearing	3	24
Hypertension	1	23
Nervous System	14	55
Gastrointestinal	3	13

Special Study in New Jersey Plant Producing Malathion

Cooperative arrangements were made with a large plant for Dr. Arthur E. DePalma, at the time, Principal Investigator of the New Jersey Project, to examine past personnel and medical records of a group of employees who worked directly with organic phosphates, Malathion in particular, for a long period of time. This company has a medical department, where medical examinations and other pertinent testing are conducted on a regular basis. This plant is what we would term a "clean plant," in that housekeeping is excellent and protective equipment and protective measures are good. The workers examined were long-time employees; some going back 15 years or more. Production of Malathion started in 1951.

In an examination of the medical histories of 34 men, the following information was obtained:

Skin (20 incidents), and particularly eye irritations (237 incidents), were frequent but they seemed to lack chronic sequelae. Monthly cholinesterase testing was generally normal, and occasionally, when abnormal, the particular individual was transferred out of organophosphate work. One case of systemic poisoning was found. Eighteen respiratory tract irritations were noted. Eight of the men revealed hypertension in more than one examination.

In summary, in this plant there were definite indications of a high incidence of skin and eye irritations, some respiratory tract irritations, some cases of hypertension, and one case of organophosphate poisoning. Aside from this, there were no other indications that these 34 men were suffereing from any chronic adverse health effects.

Dr. Reich's Study of 1969 Data

Dr. George A. Reich, in analyzing data printouts of 1969 subset information generated by Mrs. Janet R. Daling from the State of Washington, found that in a group of 741 workers, 311 had a total of 411 reactions to pesticides.[1] The greatest number of reactions resulted from exposure to the organophosphates. Ninety-three reactions were reported as a result of exposure to parathion. Symptoms reported, some of which are shown in Table 6, were: headache, nausea, dizziness, dermatitis, tearing, rhinitis, blurred vision, vomiting, fatigue, muscular weakness, difficult breathing, abdominal pain, and a few others.

TABLE 6

Major Symptoms Reported Due to Pesticides Among Workers

Chemical Class	Reactions*	Symptoms Occurring In 10% or More of Cases
Chlorinated Hydrocarbon Insecticides	68	Headache Nausea Dizziness Dermatitis
Chlorinated Hydrocarbon Herbicides, etc.	32	Dermatitis Rhinitis Tearing Headache
Organophosphates'	243	Headache Nausea Blurred Vision Dizziness

*Only chemical classes with at least 10 cases are included.

Some Published Reports on Other Studies of Pesticide Workers

A study was made by Dr. A. P. Poland, et al of 73 employees in a 2,4,-D and 2,4,5-T plant.[2] These compounds are organochlorine herbicides: dichloro- and trichloro-phenoxyacetic acids.

Chloracne was found (moderate to severe lesions) in 18 percent of the workers. Sixty-six percent more had some degree of acne. No clinical porphyria could be currently found, and one worker had persistent uroporphyrinuria. No systemic toxicity differing from normal populations was found. We have received information from a law firm that most of the former employees of this plant, which is now out of business, have filed Workmen's Compensation suits against the company.

A report was made by I. Hoogendam, et al, on a health survey of 300 workers in plants manufacturing aldrin, dieldrin, and endrin (toxic organochlorine pesticides) over a period of up to nine years.[3] Although no fatalities and apparently no permanent damage occurred, 17 of the workers had convulsive intoxications, and five of the 17 had more than one convulsion.

Nine cases of convulsions in pesticide workers handling Thiodan, a highly toxic chlorinated hydrocarbon insecticide, are reported in a paper by Dr. Thomas S. Ely, et al.[4]

Dr. I. R. Tabershaw, et al, made a follow-up study of 235 individuals three years after acute organophosphate poisoning.[5] Of this group, 114 had clearly defined organophosphate poisoning. Forty-three of the 114 had complaints for more than six months after poisoning, and 33 still had complaints three years after intoxication. These complaints were in the following categories: optic, headaches, chest pains, shortness of breath, cardiovascular, neuropsychiatric, and miscellaneous.

Environmental, clinical, and biochemical evaluations were made by Dr. M. Wasserman, et al, over a five-year period, on pesticide workers in a pesticide manufacturing plant in Israel.[6] The report is based on data obtained by using the Cornell Medical Index Questionnaire. One hundred and forty workers in the pesticide manufacturing plant were compared to 71 workers from a textile plant as the control group. The results indicated:

1. There was a high incidence of complaints in the pesticide workers group.

2. Both groups demonstrated similar frequency of complaints in those sections relating to mood and feeling patterns.

3. Higher incidence of positive answers in the pesticide group, as far as the respiratory, cardiovascular and nervous systems are concerned.

4. In both groups, the number of complaints increased with age.

Table 7 lists positive answers to various sections of the CMI.

TABLE 7

Positive Answers in CMI According to CMI Sections

Sections	Positive Answers (Mean) PMP*	Control	Probability
Eyes and Ears	1.05	0.86	$p > 0.10$
Respiratory System	1.81	1.07	$p < 0.03$
Cardiovascular System	1.28	0.74	$p < 0.01$
Digestive System	3.27	2.48	$p < 0.05$
Musculoskeletal System	0.94	0.67	$p > 0.10$
Nervous System	1.77	1.15	$p < 0.03$
Genito-Urinary System	0.92	0.76	$p > 0.10$
Fatigability	1.13	0.87	$p > 0.10$
Frequency of Illness	0.72	0.39	$p = 0.10$
Miscellaneous Diseases	1.11	0.77	$p < 0.10$

*PMP - Pesticide Manufacturing Plant.

Dr. T. H. Milby, et al, reported on blood examinations of 40 people working in a lindane plant, compared to 40 unexposed controls.[7] The following significant differences were found: creatinine, reticulocyte count, white blood cell count, polymorphonuclear leukocyte count, and blood lindane count. Although the differences were significant, only one fell outside the normal range--the blood lindane.

In a report by G. G. Mikailova, poor sanitary and hygienic working conditions and personal protection in working with many pesticides (organochlorine and organophosphates) has led to functional disorders of the nervous system, coupled with the appearance of anemia and disorders in the enzyme systems.[8] Abnormalities were also reported in the protein-forming functions of the liver.

CONCLUSIONS.

In summation, there is data on hand now to state that pesticide-exposed workers in pesticide plants differ from minimally-exposed controls in a number of parameters:

1. Abnormal cholinesterase (low) and abnormally high organochlorine residues in sera.

2. Blood Biochemistry - Higher rate of abnormals in glucose, uric acid, cholesterol, calcium, LDH, alkaline phosphatase, SGOT, SGPT, CPK, creatinine, and albumin.

3. Probable renal and hepatic dysfunctions, caused by excessive exposure to pesticides.

4. Morbidity, in the following categories: back trouble, chronic cough and sinusitis, dizziness and headache, hearing, hypertension, nervous system, gastrointestinal, cerebrovascular, cardiovascular, nephritis and nephrosis, dermatitis.

Occupational health hazards as a result of heavy exposure to pesticides are the rule and not the exception in most pesticide plants. Where protective measures and plant and personal hygiene are good, and this is the exception, exposure to the less toxic pesticides can be held to a minimum. However, it should be pointed out that no matter how good plant protective measures are, exposure to the more highly toxic pesticides, such as parathion, phosdrin, etc., is hazardous to the health of the pesticide worker.

5. Acute pesticide intoxications and sequelae - The number of acute cases of pesticide poisoning and the frequency of subacute cases far exceeds those reported in the general population.

Further research and investigations are necessary to confirm what has been found to date, and to relate the subtle effects of repeated pesticide insults on man's health to chronic disease states.

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THE INVESTIGATION OF A FIELD PROBLEM OF AN UNKNOWN ETIOLOGY

EARL EDSEL MOORE

This paper will be primarily directed to pesticide-environmental incidents and situations, but occasional reference will be made to pesticide human exposure considerations.

The safe and proper use of pesticides is of major interest to everyone and especially to those State and Federal Agencies with pesticide regulatory responsibilities.

These agencies must deal with a multitude of situations that may involve contaminated foods, goods, environmental or other detrimental conditions. It is, therefore, imperative that swift and proper action be implemented to adequately safeguard public health and for the preservation of a quality environment.

The proper documentation of pesticide accidents and incidental contamination, as a result of faulty or indiscriminate use, can serve as a useful basis for developing preventive measures in pesticide use considerations. The facts uncovered by a thorough investigation of a pesticide oriented problem can be translated into vigorous educational programs.

Numerous incidents and dilemmas occur yearly in which a pesticide is implicated or suspect. There may be accidental human exposures, occasionally resulting in death, crop damage, fish and wildlife kills, a contaminated water supply, a contaminated livestock feed, and many other related incidents.

It should be clearly understood there is no magic formula in conducting field investigations that would apply to all circumstances, as there are too many variables and possibilities. For instance, the investigation of a pesticide human exposure would necessitate a different approach than, perhaps, an environmental occurrence. However, there are certain basic principals that can be observed and applied when a pesticide is implicated or suspect.

A thorough epidemiological investigation should determine the who and what was involved. The who (host) may be man, animals, wildlife, water supply, crop, etc., and the responsible agent (what? pesticide), and the environmental situation which may have contributed to the occurrence of the incident, (such as pesticide misuse, improper protective clothing, runoff in a water supply, spray drift, or whatever the case may be).

Proper evaluation of the information gathered in an investigation can serve as an instrumental tool in developing programs to abate reoccurrences.

These have been employed very effectively for decades by public health agencies in the control of communicable diseases, foodborne outbreaks, epidemics, chronic disease and others.

It is most essential to understand that all pesticides are toxic chemicals and, by necessity, are poisonous in order to kill pests. They are capable of producing illness of varying degrees and even death to man, animals and wildlife when indiscriminately used. The extent and severity of morbidity or mortality will depend on numerous factors, including the toxicity of the pesticide, route of exposure (oral, dermal, respiratory), the susceptibility or sensitivity of the person (s), animal (s), or wildlife involved and others. Individual reactions will also vary depending on environmental factors such as temperature, humidity, and diet, and intrinsic factors such as age, race, sex, physiological activity, subclinical pathology, fatigue, etc.

In simple terms, this implies all living creatures possess a different sensitivity level as to the degree of exposure that produces or constitutes illness or death.

In retrospect to these variables, trends are somewhat apparent in most human or animal poisonings or environmental investigations. The time interval between exposure and the onset of symptoms (the incubation period) is generally short. Naturally, this is much more pronounced where humans and animals are involved. By the same token, a defoliant herbicide drifting on a tobacco or tomato field would produce adverse effects rapidly.

The manifestation of most acute exposures to humans will produce symptoms within a few minutes (there are, of course, exceptions, for instance Paraquat, a defoliant herbicide has an incubation period of 7 to 21 days). As expected, a concentrated solution will produce clinical symptoms more rapidly than a diluted one, and an oral exposure will generally produce earlier signs than a dermal exposure.

An investigation of a human poisoning and particularly, occurrences involving foods and environmental contamination may necessitate the cooperation of several people and/or agencies. Most important is the cooperation and support of a competent toxicology laboratory that has the capability to perform pesticide residue detection. Most investigations, especially those of an environmentally oriented nature, will require the collection of samples for analysis, for without adequate sampling of specimens and a reliable analysis very little may be accomplished.

Considerations in Conducting Pesticide Field Investigations.

Perhaps, one of the most important points to emphasize is the investigation should be inaugurated as soon as the incident is reported for several reasons:

1. This practice may enhance an opportunity to witness the actual condition (s) or situation. For instance, spray drift from an airplane may have caused crop damage and of less significance than reported. There may be other extenuating circumstances to the problem.

2. Presents a better opportunity of gathering all the details encompassing the incident. Memories are often short and important points may be overlooked should sufficient time elapse.

3. In the event the incident warrants the collection of environmental sample (s), it is likely the sample (s) will be of more value than if a significant amount of time has elapsed. The situation may be subject to change, depending on the environmental conditions (there may be instances when the investigator is handicapped because of delayed reporting). For example, a report is received that an airplane had sprayed chemicals on a crop near a farm pond and there was suspicion of drift. There was no visual evidence of fish mortality and livestock drank the water without ill effects, yet three weeks elapsed before the incident was reported. In such instances it may be impossible to establish a hazardous condition ever existed. This, of course, would be contingent on the persistence of the chemicals used.

4. The investigation should be detailed and thorough, especially those involving environmental situations. There may be subsequent legal action and the investigator may be subpoenaed to testify in court and the report of the investigation (or portions) may be introduced as admissible evidence in the proceedings. The investigator should be generally acquainted with state laws and regulations applicable to pesticides. The investigation should reveal any infractions that may have occurred. For instance, a custom applicator may be involved in an incident and it was determined he was not properly licensed.

5. When determined applicable, camera snap shots, preferably color slides (Polaroid may be suitable in certain situations) are an excellent illustration of property damage and actual conditions at the time of the investigation.

6. The investigator should always be prepared to collect samples for pesticide analysis if applicable. It may be feasible to determine the necessity at the time of reporting and the appropriate tools and type of containers required for collection. This would depend largely on the nature of the incident. Samples for analysis should never be accepted from an unauthorized person or agency. (They would not be acceptable should legal proceedings subsequently develop). The laboratory should be alerted that samples may be collected for analysis in order to acquire the results as soon as possible following submission of samples. The important point is that samples should be collected and analyzed as soon as possible. This can be accomplished if the investigator goes prepared and communicates with the laboratory.

The investigator may find it desirable to attempt to determine the agent (Pesticide) involved or suspected at the time of reporting. This would present an opportunity to become familiar with the classification and toxicity and other characteristics of the chemical,such as persistence, which may be of value in conducting the investigation. For example, a farm owner reports an aerial applicator sprayed mosquitoes with Malathion near his farm pond and two weeks later the fish suddenly died. The investigator then should consider and look for other causative agents because Malathion has a low order of toxicity and is nonpersistent.

What then, is the type of information to be documented and what should the investigator look for, questions to ask and data to record? This is somewhat dependent on the nature and severity of the incident. It is likely environmental incidents will require a more comprehensive investigation and consequently, the discussion is directed accordingly. Reports should be written promptly, and the investigation and occurrences should be listed in sequence. The development of a form or format in collecting the information would be helpful.

This is not construed to be a complete listing nor necessarily in order of priority.

1. Record the date of occurrences of the incident, the exact time it is reported and by whom, their phone number and address. Request specific directions to the scene to prevent any unnecessary delay.

2. Contact the local health agency or other state or federal agencies that may also have some responsibility to the problem (transportation spillage accidents, fish kills, contaminated food moving in interstate commerce, etc.). In certain instances, when a causative agent is suspected and represents a detrimental effect, the investigator should be prepared to advise a quarantine (pending on investigations and a laboratory analysis of samples), provided, the person reporting the incident has the authority to invoke such action to abate further contamination or hazardous conditions.

3. After arriving at the scene, should more than one individual be acquainted or have knowledge of the incident, interviewing all connected persons should enhance a better representation of what developed and transpired. Secure names, addresses, and phone numbers, as it may be necessary to re-establish contact at a later date to clarify a point.

4. Describe the nature of the problem and record the environmental situation (s) encompassing the incident. (If applicable).

5. Attempt to determine the source of contamination and the causative agent (s) as soon as possible. This may be very important in preventing further possible detrimental effects. Appropriate specimen collection apparatus should have been brought along.

6. For on-the-farm problems (such as a livestock kill, crop damage, or contaminated feed stuffs) record the pesticides or toxic agents that have been used recently and last date of application, rate and method application. It may also require securing similar information from a neighbor (s) to determine who is at fault.

7. The evaluation of habits of pesticide usage, storage, (where and how) and disposal of empty containers may be of value in determining the cause of the incident and possibly where the fault lies.

8. In instances when a pesticide is suspect or implicated, record name of pesticide, formulation, active ingredients, manufacturer, size of container, amount used. This will be important in checking for cross contamination and also, perhaps, for checking proper instate registration. A copy of the label of the actual container may be helpful. Secure a copy of invoices, bill of lading, or any other document which may be associated with or conceivably have bearing on the incident.

9. List species of animal (s), wildlife, crop (s), or portion (s) of the environment affected. Record the visible effects as they exist and are observed.

10. Record route of exposure to animals or wildlife (dermal, oral, respiratory) and directly or indirectly such as an application or consumption of contaminated goods.

11. Record time lapse between exposure and onset of symptoms in case of crops when damage began to appear in hours, days, etc., and the duration of exposure,provided this can be validly established.

12. In instances involving animals and wildlife, record the number affected, number expired, and number recovered.

13. Treatment (if any, what and by whom).

14. Upon conclusion of the investigation, should the investigator consider it <u>necessary</u> and has the authority, quarantine action should be inaugurated to prevent any further detrimental effects to public health or the environment (if not previously accomplished).

There will be other details dependent on the occurrence, as there are a multitude of variables and each occurrence in all probability will be somewhat different, nor will particular situations require collection of all of the suggested data. It should be emphasized that often the investigator <u>fails to document sufficient detailed information</u> when conducting the initial investigation, usually necessitating a return visit. Since conditions are subject to change, it is imperative to conduct a thorough investigation on the initial visit.

The proper sampling of specimens for pesticide analysis is extremely important, for without a representative sample (s) collected in the proper amount, in the prescribed manner, and the appropriate container, it will be of little value. The source of the problem may not be determined. In fact, the success of the investigation may impinge on the samples collected. Only brief reference is made to specimen collection as "Sampling Procedures" are scheduled for discussion later in the course.

1. All specimens should be placed in chemically clean containers provided by the testing laboratory. (Never put specimens for pesticide analysis in plastic containers). If applicable, use chemically clean tools (scoop, bucket, cup, etc.) in collecting the specimen (s).

2. The sample should be representative of the contaminated media.

3. All samples should be properly identified.

4. Provide the laboratory analyst with a brief resume of the incident and, if possible, a clue to the pesticide (s) to analyze for. Remember, the analyst does not have the benefit of the knowledge of the investigator.

5. Submit the samples as soon as possible after they are collected. Residues are subject to degradation the rate of which is dependent on the pesticide involved.

To emphasize the value of gathering detailed information and drafting a comprehensive report, the following are reports of two actual investigations illustrating the importance of many points that have been discussed. These may also serve as an aid in conducting investigations of a similar nature.

ABSTRACT OF A FIELD INVESTIGATION TO LOCATE A CONTAMINATED DAIRY HERD AND ISOLATE SOURCE OF CONTAMINATION

This is an account of an investigation and subsequent developments of an actual occurrence to locate a dairy farm producing a contaminated milk that was being shipped interstate to the Cincinnati, Ohio Milk Shed in April 1969 and to isolate the source of the contamination. The names and firms of those involved in this investigation have been excluded.

The investigation reflects a sequence of events by both the Food and Drug Administration and the Kentucky State Department of Health.

On April 2, 1969, the Cincinnati Regional Office of the United States Food and Drug Administration notified the Kentucky State Department of Health that a violative level of Dieldrin (a toxic chlorinated hydrocarbon insecticide) had been detected in a sample of large curd creamed cottage cheese, manufactured by a local firm. The discovery occurred as a product of the Food and Drug Administration's Established Routine Food Basket Survey and Surveillance Program (compliance of permissible pesticide residues in foods). A Food and Drug Official disclosed the detection occurred on March 16, 1969, and that subsequent investigations revealed the source of contamination was fluid milk originating from a route that involved 12 Central Kentucky milk producers. Furthermore, a Food and Drug Administration Inspector had been dispatched to begin sampling individual producers on the route on March 31 to determine the source (s) of contamination.

On April 3, a State Department of Health Investigator,accompanied by the milk hauler covering the route, began sampling of the 12 milk producers on the route,in a cooperative effort with the Food and Drug Administration, to determine the source (s) of contamination. The samples were submitted to the State Department of Health Pesticide Laboratory for analysis the same day.

While collecting the milk samples from the 12 farms, a detailed inquiry regarding pesticide usage on the farms during the last year indicated there did not appear to be any misuse or faulty storage.

Meanwhile the Food and Drug Administration had advised the Cincinnati Department of Health of the problem. The Kentucky State Department of Health, the Food and Drug

Administration, and Cincinnati officials collaborated, and accordingly placed the 12 farms under official quarantine, preventing further shipment and sale of the milk either interstate (March 31) or intrastate (April 2).

In the late afternoon of April 3, Food and Drug Officials notified the State Department of Health that samples collected by their field inspector from the milk producers were free of contamination except one. The sample was from a producer with a 105 cow herd. A few feed samples collected on the farm on March 31 by the Food and Drug Administration were reported void of contamination. Thus, the contaminated herd was isolated.

The quarantine on the remaining 11 herds was rescinded on the evening of April 3 by the State Department of Health.

Due to the high level of Dieldrin in the milk of the affected farm, the investigator revisited the farm on April 4 to sample all feeds in inventory, water, and forage to which the milking herd had been exposed, to determine the source of contamination and prevent further contaminations. The samples were submitted to the State Health Department Pesticide Laboratory the same day. During the revisit, the proprietor of the farm reiterated that neither Dieldrin or Aldrin (metabolized to Dieldrin by the human and animal body) had been used on the farm, and that pesticide application was accomplished by a custom applicator on crop land far removed from areas in which the producing animals had access.

Furthermore, the investigator was advised that the farm had purchased 35 head of dairy cattle and most had been incorporated into the milking herd about February 28.

The milk samples collected on the 3rd by the investigator were reported to be free of contamination, except one, by the State Health Department Pesticide Laboratory, which contained a comparable level of Dieldrin (as reported by the Food and Drug Administration).

The herds were segregated on April 5 to determine the feasibility of the new herd being the contaminating source. A composite sample from each group revealed the level to be comparable, indicating that either or both a feed item or water must be the contributing source.

On April 15, the laboratory reported all feed, water, and forage samples collected on the farm were void of any Aldrin or Dieldrin contamination. Subsequent milk samples from the combined herd on April 10 and 11 revealed the level of Dieldrin to be declining, indicating the animals were not being subsequently exposed. Consequently, it could be concluded that a contaminated feed must have been fed prior to March 31, 1969 (the day the Food and Drug Administration collected samples of farm feeds, etc.).

The milking ration for the dairy herd was prepared on the farm and numerous ingredients were purchased from several sources and rather frequently, in fact, all of the raw ingredients sampled on April 4 had been in inventory for 10 days or less (except a small quantity of ear corn purchased in Indiana). These were transported to the farm in the farm truck.

During a revisitation to the affected farm on April 16, the proprietor of the farm disclosed the source of two of the raw ingredients (bagged soy bean and cotton seed oil meal) was purchased from a local grain firm that retailed and warehoused pesticide products. This was not the case with the other two sources of ingredients. It was suspicioned that possibly as a result of faulty warehousing or handling that raw ingredients purchased from the firm may have been accidentally contaminated. An inspection of the facilities failed to indicate this feasibility.

The visit and inspection, however, proved to be valuable. The manager of the firm disclosed that the affected farm had purchased a quantity of feed oats for incorporation in the milking ration, but from another local grain supplier that was the low

bidder. Furthermore, the oats had been purchased prior to the detection of the contaminated milk by the Food and Drug Administration.

A visit with the manager of the local firm, reportedly supplying the oats, verified the purchase but that the firm had acted only as the intermediary in the transaction. Three hundred bushels of oats were purchased on February 28, 1971 from a Louisville based grain elevator, delivered the same day to the affected farm in a truck owned by the local firm. The purchase invoice, however, bore the name of the local firm.

Returning to the farm late the 16th, the proprietor admitted that mention of the oats had been overlooked during the initial investigation. The oats had been incorporated into the milking ration beginning about March 3 and the supply exhausted about March 25th. Furthermore, it was believed none of the oats remained in inventory, however, an inspection revealed there was some eight to ten bushels in the storage bin.

A representative sample from the lot was collected and submitted to the Kentucky State Health Department Laboratory and subsequently, reported to contain a violative level of Aldrin. Thus, the contaminating source was officially isolated by the Health Department on April 28, requiring some 24 days (April 4 - 28) in the process. Hence, the initial and subsequent investigations were an important basis to determine the actual period of contamination of the herd (March 3 through March 25), and the amount of contaminated milk that was marketed. The time period of March 4 (in all probability when the Dieldrin began to appear in the milk) and March 31, when the quarantine became effective. It was calculated some 108,000 pounds of contaminated milk were marketed (27 days, herd average 4,000 a day).

Since the oats contained a violative level of Aldrin, and also subject to provisions of the Kentucky Food, Drug and Cosmetic Act, further investigation was required.

An investigation of the originating source of the oats, a Louisville grain elevator, was begun on April 28. Approximately 10,600 bushels were in inventory and were promptly placed under quarantine. Officials of the firm believed the 300 bushels purchased by the affected farm may have been a part of approximately 30,000 bushels of oats that had been received between February 11, 1969 and April 1, 1969. The oats were procured from a grain elevator in Indiana and reportedly came from several growers over a multi-state area prior to and during the time period specified above. Nineteen thousand bushels of the lot had been sold almost exclusively to three poultry farms in North Carolina and Georgia. Other than the oats in question, less than a hundred bushels had been sold locally.

Representative samples from six bins from which oats were stored were collected and submitted to the State Health Department Pesticide Laboratory for analysis. On May 5, the Pesticide Laboratory reported the oats to be void of contamination. Consequently, it was impossible to establish what portion of the 30,000 bushels were contaminated. Because of elapsed time between purchase of the oats by the affected farm and detection as the contaminating source (February 28 through April 28), Food and Drug Administration Officials in North Carolina and Georgia (which had been alerted on April 28) disclosed that interstate investigations did not uncover any contaminated oats. Adulterated foods or feeds moving in interstate commerce are the responsibility of the Food and Drug Administration.

The quarantine on the oats in inventory was rescinded on May 5 by the State Department of Health.

The affected farm was required to destroy the milk produced from the herd covering an 84 day period (March 31 through June 22) or until the level met the zero tolerance established by the Food and Drug Administration. The milk producer experienced a substantial loss during this time period which amounted to approximately $24,000.

Since the State Health Department investigation revealed the farmer was not at fault, because of faulty use or storage, he was eligible for restitution for a portion of the loss through a federal government disaster program. Additionally, the Cincinnati Milk Shed absorbed a portion of the loss, however, combined, both were not sufficient to account for the entire loss suffered by the producer.

The producer subsequently instigated legal proceedings against the local grain firm and the Louisville grain elevator for restitution for the remainder of the loss of the milk.

Council for the defendants reviewed the dossier of the investigations, laboratory analysis, and all other pertinent information encompassing the incident. The attorney disclosed the evidence would disfavor his clientele in court. Consequently, the deficit, (some $1,650) was remunerated to the milk producer.

An experimental trial coordinated by the Department of Animal Science, University of Kentucky, of feeding phenobarbital and activated carbon, was apparently effective in accelerating removal of Dieldrin in the 105 cow dairy herd.[1/] The herd was divided into two groups. After one week of treatment, residue had declined about 64% compared with 36% for the control group. The time during which the milk had to be withheld from the market was shortened by at least one month for the treated group.

AN ABSTRACT OF A FIELD INVESTIGATION TO DETERMINE THE CAUSATION OF MORTALITY IN A BEEF HERD

During the late afternoon of August 19, 1970, the Director of the Kentucky State Department of Agriculture's Diagnostic Laboratory notified the Kentucky State Department of Health that a small Western Kentucky beef cattle producer had mysteriously lost 14 head of breeding stock in less than a 24 hour period. Additionally, the herd veterinarian was unable to establish the cause for the sudden mortality which occurred on August 18. However, the veterinarian felt a toxic material was involved after performing an autopsy. Furthermore, there was suspicion that a stream running through the farm from which the animals drank was contaminated with a pesticide.

The affected producer disclosed in the investigation instigated on August 20, that on checking the herd on the morning of August 18, ten animals were found dead in the pasture field, four were very ill, eight others appeared to be slightly ill, and the remainder appeared normal. They were droopy, lethargic, generally weak, ataxia, and had diarrhea. It was reported the other sick animals died later on the 18th and had tremors and muscle twitching, in addition to the above symptoms. According to the owner, a treatment of atropine sulphate was administered by the herd veterinarian which is the treatment or antidote for poisoning by organo phosphate and carbamate insecticides. However, the ill animals failed to respond, and it was later discovered that this was an improper treatment. It could not be determined what effects, if any, this constituted to the other recovering animals.

The owner disclosed that pesticides had not been applied to any fields or forage (the only diet) to which the animals had been exposed. Samples of forage from the pasture field and from the suspect stream were collected for pesticide analysis. Adjoining farm owners, with cattle drinking from the same stream, reported no sick animals or losses.

An inspection of pesticide storage on the affected farm revealed a few pesticides which were occasionally used on field crops, mainly tobacco. A half gallon container of Toxphene was noticed, which no longer is recommended for tobacco. The owner disclosed that the insecticide was purchased on August 15 from a local firm for the purpose of spraying the cattle for fly control, and had used Toxaphene for several years without any ill effects. Less than a quart had been used, and he was sure this was not the causative agent.

The cattle had been congregated on the 17th, however, 12 were not sprayed because of darkness. Ill effects were not noticed until the next day and because of the illness and death in the herd, the owner decided not to spray the remaining cattle.

The owner stated he had followed label directions on the Toxaphene container with the exception of incorporating approximately a half gallon diesel fuel with the spray mixture to enhance the residual period (only water was recommended).

The supposedly diesel fuel had been poured from an unlabeled one gallon, brown colored glass container. However, an inspection did not reveal the type of odor or exact appearance.

A sample was collected from the Toxaphene container to analyze for possible cross contamination as a result of faulty manufacturing. Samples were also collected of the spray mixture remaining in the spray tank, the one gallon container, and specimens from two organs of one of the expired animals.

The animals were quarantined pending laboratory analysis to determine the causative agent. This was a safeguard to prevent ill animals from being marketed.

On August 27, the Pesticide and Chemistry Laboratories reported the samples of forage and water were void of contamination and the Toxaphene was not cross contaminated. Furthermore, the spray tank sample and especially the gallon glass container (supposedly diesel fuel) contained high levels of arsenic. The tissues also contained a lethal level.

It was subsequently established that Sodium Arsenite was the pesticide in the unlabeled glass container.

The spray solution apparently caused skin irritation, consequently, the cattle licked their coats ingesting lethal levels of the arsenic containing compound.

In a later discussion, the owner denied purchasing the pesticide, much less storing in an unlabeled container. Furthermore, that he had personally procured the gallon of diesel fuel and put in the unlabeled container and stored in the exact location as the contaminated container. The owner declared since sodium arsenite was found someone had maliciously switched containers.

The fact remains, had the farm owner strictly adhered to the label directions, the incident would not have occurred. The loss of the cattle was estimated at $4,000, indeed an unfortunate and expensive mistake. Since the incident was a result of misuse, the producer was not eligible to receive restitution from any disaster programs.

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SAMPLING PROCEDURES

Bill L. Stevenson

To promptly and accurately evaluate chemical pesticides in biological and environmental media, suitable representative samples of these systems insure quality analytical performance.

The identification and evaluation of pesticides present in samples submitted to a laboratory may serve as a basis for the documentation of an accident or incidental contamination from normal use. Laboratory data is a necessity to identify current and potential public health problems and protect the environment from unanticipated contamination.

Data from a competent laboratory based upon improper sampling can lead to false conclusions concerning the pesticide profile of the sample even though properly analyzed. For example, let us assume that a laboratory making routine blood analysis of the general population in a given area is consistently, but erroneously, finding higher pesticide levels than is being reported by similar laboratories in other areas. Plotted on a national scale, it would then appear that the people of this area are being exposed to higher levels of pesticides than the rest of the national population.

Another example can be cited which involved complaints filed by several women employees making draperies for mobile homes that some irritant was present in the atmosphere. An investigation was made and a survey of the work area revealed that the entire operation, including the storage of bolts of drapery cloth, was confined to a room 12' x 15' with a 3/4 ton air conditioner providing the only ventilation.

Through a literature review, it was learned that formaldehyde is used to make colors "fast" in the dyeing process of cloth. This information indicated a possible source of the problem.

The sampling procedure followed (to determine exposure levels to atmospheric formaldehyde in work areas) was recommended by an excellent and authoritative source. However, one small but important detail was omitted in the sampling instructions--that was to use an impinger with a diffusion attachment to disperse the air stream into tiny bubbles for greater absorption in the collection media. This omission resulted in a false reading indicating a safe working environment when in fact, the formaldehyde vapors exceeded established threshold limits. A law suit was instituted and was an embarrassment to all concerned.

Interferences are encountered in most analytical methods; therefore, it is rare that a method is free from all interferences regardless of the concentration of chemicals in a sample. Nevertheless, most methods will yield reliable results with little interference when followed as presented by authoritative and approved methods.

Analytical procedures are usually designed either to give the total amount of an element present in a sample or to give the amount of a certain definite solute species. Interferences affect either type of analytical procedure and the results are a serious potential source of error against which the analyst must always be aware.

The following general rules for sampling can be utilized in most investigations:[1]

1. Never take a composite sample unless the subject area to be sampled is known to be uniformly contaminated.

2. Take a number of samples from the subject area that would best represent possible areas of contamination.

3. Take the samples immediately, when reason for concern is apparent. It may be too late - later.

4. Label the samples with all the information immediately. You may forget later.

5. Preserve the samples with whatever means are necessary. This may be refrigeration, freezing, formaldehyde or solvent.

6. Make sure the means of preservation is compatible with subsequent analysis. Samples of crab eater seals and penquins from the Antarctic were shipped back to this country wrapped in plastic. As a result the reported levels of DDT are questionable due to the plasticizer in the plastic. Don't preserve samples to be used for chlorinated hydrocarbon analysis with chloroform. Don't preserve samples for phosphate analysis with formaldehyde. If you don't know what analysis will be required, refrigeration is your best bet.

7. Take a large enough sample. Tomorrow will be too late to get more.

8. Be prepared to take samples. Have sampling tools needed, knives, scissors, trowels, spoons, etc. Have suitable bottles for samples.

9. Label all samples.

10. Write a description of the situation as the investigator sees it at time of sampling. It is not unusual for the cost of analysis in particular investigations to run $10,000. This expenditure should not be jeopardized because the sampler is too lazy to write down the situation as he sees it. Provide a case history. This is needed for the chemist to get a clue as to what to analyze for. He cannot possibly screen for the million or so compounds that presently contaminate our environment.

11. Get samples to laboratory <u>now</u>. Don't wait two weeks while you talk the situation over.

<u>Procedures for taking samples</u>:

Although pathologists should have adequate knowledge concerning the collection and submission of autopsy samples for chemical analysis, occasionally samples are contaminated by using improper containers or solutions that interfere with analytical methods.

Samples from suspected human poisonings:

1. Quantity:

   a. Tissue - 1-5 grams
   b. Vomitus - 2 ounces or more
   c. Stomach content - 2 ounces or more
   d. Stomach wall tissue - 5 grams or more
   e. Kidney - 1-5 grams
   f. Liver - 1-5 grams
   g. Blood - 5-10 ml
   h. Urine - 5-10 ml
   i. Brain - 1-5 grams

2. Packaging: Each tissue sample should be isolated in a separate chemically clean glass jar or bottle.

3. Shipment: It is preferable to have the samples frozen and shipped on Monday to the appropriate laboratory. When samples are frozen, care should be taken that enough dry ice is included to insure arrival of samples in a frozen condition.

Soils: The area should be searched carefully for oil spots or areas that look different from the surroundings. These can be sampled by using a sampling tool made from a tin can or similar container. Cut both top and bottom out evenly. Wash well and repeatedly. Rinse in clear water. Press this can in suspect area to depth of 1-1/2 - 2 inches and remove from soil. Punch core taken into new quart mason jar. Take several more cores from same areas. Seal jar and send to the laboratory after careful marking to indicate where sample was taken, when, by whom, and number and depth of cores.[1]

Water: Water samples should be submitted in chemically clean one-gallon glass bottles.

Most natural water bodies are not completely homogeneous, and obtaining a truly representative sample will depend on the sampling technique employed, as well as the size and number of samples collected.[2] Proper sampling of large bodies of water should include a surface sample, an intermediate sample and a bottom sample. Always use chemically clean glass bottles for collecting samples.

Interfering elements are leached from plastic; therefore, plastic sample bottles should never be used to collect samples for pesticide analysis.

Swab Samples: Sampling to determine contamination on a wall or duct or other surfaces may be collected through the use of sterile wool, some medical alcohol or acetone and plastic throw away gloves. Wearing the gloves, wash the suspect area with swabs of cotton and solvent using care not to let solvent squeeze out of the swab. Place used swab in pint mason jar. Repeat on adjacent area. When labeling bottle, record where sample was taken, by whom, how it was sampled and how large an area.[1]

The following tables provide information for proper sample collection; i.e., size of sample, packing storage, preservatives and other helpful information.[1]

BIBLIOGRAPHY

1. Barthel, W. F., Sampling Procedures for Chemicals in the Environment, Atlanta Toxicology Branch, Division of Pesticide Community Studies, Environmental Protection Agency, Chamblee, Georgia.

2. Brown, Eugene; Skougstad, M. W. and Fishman, M. J., Methods for Collection and Analysis of Water Samples for Dissolved Minerals and Gases.

AIR SAMPLING

Sampling of air requires sophisticated equipment and methods. Consult State Services Section for information.

OTHER SAMPLING

Many other types of sampling are occasionally required such as grain, feed, flour, food or other types of samples representing human or animal exposure. It is highly important in such cases to inspect carefully the material to be sampled in order to detect possible areas of contamination. Sometimes only one sack in a shipment will show an oily spot of contamination, or the colored grain denoting seed treatment. Samples should be drawn both from suspect and non-suspect areas and so labeled. If in doubt, call the appropriate laboratory for guidance.

LABELING AND SHIPPING

Without proper labeling or shipping, all the care and trouble of taking the samples is wasted. Be sure the label is explanatory and well attached. Ship samples on a Monday so that they arrive during the week and not over the weekend where they might sit in a hot airport terminal and deteriorate. If the samples are worth taking, they are worth packing well and with a little extra dry ice or other refrigerant.

Attachment A

Type	Poison Examples	Types of Samples Needed
Chlorinated hydrocarbons	Aldrin Dieldrin DDT Endrin, etc.	Stomach and its content, vomitus, kidney, liver and fat.
Fluorinated compounds	1080 Sodium fluoride	Stomach and its content, or vomitus if present, liver, kidney and heart.
Inorganic phosphides	Zinc phosphide	Stomach and its content, vomitus, liver and spleen.
Organic phosphates	TEPP Parathion, etc.	Stomach and its content, vomitus, brain, heart, blood (if not deteriorated).
Phosphorous	Elemental phosphorous	Stomach and its content, vomitus, liver and kidney.
Cyanide	Cyanogen Sodium cyanide	Stomach and its content, vomitus, throat tissue, heart, brain and lung tissue.
Alkaloids	Strychnine	Stomach and its content, vomitus, liver and kidney.
Thallium	Thallium sulfate	Stomach and its content, vomitus, liver, kidney, leg muscle and bone.
Cardiac glucosides	Red squill	Stomach and its content, vomitus and a portion of intestine.
Lead	Lead acetate Lead arsenate	Stomach and its content, vomitus, liver, kidney, and long skeletal bones (leg).
Anticoagulants	Warfarin Pival PMP Diphacin	Stomach and its content, vomitus, heart, liver and blood.
Miscellaneous poisons, toxic compound unknown		Stomach and its content, vomitus, heart, liver, kidney, brain, blood and bone.

TABLE I Environmental Sampling

SAMPLE	SIZE OF SAMPLE	PACKING*	STORAGE	PRESERVATIVE	OTHER INFORMATION
SAMPLING OF WATER FOLLOWING INCIDENT					
private well	1 gallon	glass	ambient	none	description of well date
municipal pre filter at filter treated	1 gallon ea.	glass	ambient	none	note where and when taken
river	1 gallon	glass	ambient	none	detailed location of sampling site and date
lake	1 gallon	glass	ambient	none	detailed location of sampling site and date

Accompanying each set of samples should be a complete description of incident and all pertinent information to guide laboratory director in making analysis.

SAMPLING OF TISSUE AT AUTOPSY					
fat	1 to 5 gms	glass bottle or aluminum foil	frozen or 10% Formaldehyde		name of subject site of sample sample size date, cause of death
liver lung brain gonads spleen muscle, etc.	1 to 5 gms	glass bottle or aluminum foil	frozen	not acceptable	name of subject name of tissue sample size date, cause of death

* Where glass containers are specified they should be fitted with teflon or aluminum lining.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
		SAMPLING OF BODY FLUIDS			
urine for chlorinated hydrocarbons	**25 ml of 24 hr. sample if possible	glass	ambient	1/10% Formaldehyde	name of subject description whether 24 hr. or not
urine for phosphates	**25 ml of 24 hr. sample if possible	glass	frozen	none	name of subject description, whether 24 hr. or not.
blood for chlorinated hydrocarbon	1-5 ml plasma	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for phosphates	1-5 ml whole blood	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for cholinesterase	1-5 ml plasma	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician
	1-5 ml red cells	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician

** A complete case history should be provided with all human samples.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
		OTHER SAMPLING			
soil	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
sediment	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
wildlife birds mammals or reptiles	20 gms muscle (20 gms fat if possible)	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.
fish	20 gms tissue	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.

Analysis of one animal, fish or bird will generally tell but little. Enough animals should be sampled to provide a crossection exposure picture of the incident but certainly never less than 10 subjects.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL COMMUNICABLE DISEASE CENTER
PESTICIDES PROGRAM
ATLANTA, GEORGIA 30333

FORM APPROVED
BUDGET BUREAU NO 68-R1814

1. D100987

COMMUNITY STUDIES PROJECT ON PESTICIDES
ACUTE EXPOSURE RECORD

PARTICIPANT'S NAME

2. PROJECT CODE # ___ ___ 3. GROUP ID ___

4. AMA ID # ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

RTICIPANT'S ADDRESS (include zip code)

EMPLOYER'S ADDRESS (include zip code)

(D060) 1 ☐ URBAN 2 ☐ RURAL 3 ☐ UNKNOWN

DATE OF BIRTH	PHONE	SEX	RACE
__/ __/ __			

5. INTERVIEW DATE __/ __/ __

MARITAL STATUS:
1 ☐ Married 2 ☐ Widowed 3 ☐ Divorced 4 ☐ Single

INTERVIEWER'S NAME

PLOYER

8. SOURCE OF DATA: 1 ☐ Participant 2 ☐ Employer 3 ☐ Relative 4 ☐ Other (If other than participant, give name)

CURRENT OCCUPATION: (D010)

CODE (INDEX II) __ __

NUMBER OF YEARS __ __ (Report to nearest year)

CHIEF COMPLAINT: (D020)
(Mark (x) by any symptoms which occurred as part of the chief complaint.)

CODE

00 ☐ none	11 ☐ coma, unconsciousness	22 ☐ palpitations
01 ☐ malaise	12 ☐ skin flushing	23 ☐ nausea
02 ☐ fatigue	13 ☐ increased sweating	24 ☐ vomiting
03 ☐ confusion	14 ☐ cyanosis	25 ☐ abdominal pain, cramps
04 ☐ headache	15 ☐ blurred vision	26 ☐ diarrhea
05 ☐ nervousness	16 ☐ increased tearing	27 ☐ muscular weakness
06 ☐ hyperirritability	17 ☐ rhinitis	28 ☐ tremor, fasciculations
07 ☐ light-headedness	18 ☐ nasal stuffiness	29 ☐ convulsions
08 ☐ fainting	19 ☐ increased salivation	30 ☐ paresthesiae
09 ☐ dizziness	20 ☐ tightness in chest	31 ☐ other (specify) ___
10 ☐ dermatitis	21 ☐ difficult breathing	32 ☐ fever

PRESENT ILLNESS

11. CASE TYPE: (D030) (Mark (x) in block by appropriate answer)

1 ☐ Accidental-home 3 ☐ Accidental-occupational 5 ☐ Homicide
2 ☐ Nonaccidental-occupational 4 ☐ Suicide or attempted suicide 6 ☐ Other ___

12. DATE AND PERIOD OF EXPOSURE: (D010)

began (date) __ __/ __ __/ __ __ (time) __ __ __ __
ended (date) __ __/ __ __/ __ __ (time) __ __ __ __ (Use 24 hour clock)

13. SUSPECTED AGENT(S): (list chemical names of pesticides and solvents. If only brand name is available, record and look up chemical name later.)

NAME	FORM (E.G. DUST, LIQUID, ETC.)	CODE (INDEX II)	APPROX. AMOUNT (IF INGESTED)
	(D050)	__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm
		__/ __ __/ __ __ __ __	mgm

14. PROBABLE MAIN ROUTE OF EXPOSURE: *(D060) (Mark (x) in block by appropriate answer)*

1 ☐ oral 2 ☐ dermal 3 ☐ inhalation 4 ☐ combination or other

15. PHRASE WHICH BEST DESCRIBES SOURCE OF AGENT *(D070) (Mark x) in block by appropriate answer)*

1 ☐ unknown or not applicable
2 ☐ bought in store
3 ☐ bought from door-to-door salesman
4 ☐ chemical taken from work
5 ☐ chemical taken from elsewhere
6 ☐ applied by commercial firm
7 ☐ applied by other person
8 ☐ provided by employer for job
9 ☐ other _____

16. WHICH BEST DESCRIBES CONTAINER? *(D080) (Mark (x) by one item from each column)*

A	B
1 ☐ original container, labeled	6 ☐ paper sack or bag
2 ☐ original container, unlabeled	7 ☐ plastic sack or bag
3 ☐ other container, unlabeled	8 ☐ bottle
4 ☐ other container, mislabeled	9 ☐ can or drum
5 ☐ other (specify _____)	10 ☐ other (specify _____)

17. WHICH BEST DESCRIBES STORAGE AREA AT HOME OR AT PLACE WHERE POISONING OCCURRED? *(D090) (Mark (x) in one box in each column. (USE ONLY IF QUESTION 11 ABOVE INDICATES HOME CASE TYPE)*

A	B	C
1 ☐ locked	3 ☐ kitchen	8 ☐ below ground or floor level
2 ☐ unlocked	4 ☐ bathroom	9 ☐ 1–4 feet above ground or floor level
	5 ☐ closet	10 ☐ 4–8 feet above ground or floor level
	6 ☐ garage, shed, etc	11 ☐ 8+ feet above ground or floor level
	7 ☐ other (specify _____)	

18. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION IN THE OCCUPATIONALLY-EXPOSED? *(D100) Mark (x) for items which best describes. (USE ONLY IF QUESTION 11 ABOVE INDICATES OCCUPATIONAL CASE TYPE)*

1 ☐ unknown
2 ☐ spillage
3 ☐ equipment malfunction
4 ☐ poor ventilation of work environment
5 ☐ poor application techniques, or poor work practices
6 ☐ drift
7 ☐ too early re-entry after fumigation
8 ☐ intentional (specify _____)
9 ☐ other (specify _____)

19. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION? *D110) Mark (x) for items which best describe (THIS IS TO BE FILLED OUT IN EVERY INSTANCE)*

1 ☐ unknown
2 ☐ ate or drank from container
3 ☐ ate bait
4 ☐ ate contaminated soil
5 ☐ drank contaminated water
6 ☐ other oral source (specify _____)
7 ☐ handled container or pesticide
8 ☐ handled contaminated object (e.g. glove) (specify _____)
9 ☐ exposed to contaminated soil or water
10 ☐ other dermal source (specify _____)
11 ☐ inhalation when foam or sponge rubber furniture was present
12 ☐ inhalation when change in ambient temperature was causally related (specify _____)
13 ☐ other inhalation (specify _____)

20. DID THIS PATIENT TAKE ANY OF THE FOLLOWING DURING THE LAST WEEK? *D120)* 1 ☐ Yes 2 ☐ No 3 ☐ Unknown
(If yes, mark (x) in box by appropriate items below, and provide requested information)

	NAME	QUANTITY/UNITS, FREQUENCY (HRS.)	DATE AND TIME LAST TAKEN	
			MO. DA	TIME (use 24 hour clock)
alcohol		(D121)	___/___	____
sedatives		(D122)	___/___	____
narcotics		(D123)	___/___	____
phenothiazine tranq		(D124)	___/___	____
carbamate tranq		(D125)	___/___	____
		(D126)	___/___	____
		(D127)	___/___	____

21. HOW LONG HAD PESTICIDES BEEN AVAILABLE AT EXPOSURE SCENE? *(D130)*

1 ☐ not applicable or unknown
2 ☐ hours
3 ☐ days
4 ☐ weeks
5 ☐ months
6 ☐ years

PROTECTIVE MEASURES IN USE DURING THIS EXPOSURE: (D140) (mark (x) in block by approp. answer 111

1 ☐ none
2 ☐ rubber gloves
3 ☐ mask or respirator
type _____
4 ☐ rubber boots
5 ☐ long sleeves
6 ☐ coveralls
7 ☐ apron
8 ☐ rubber suit
9 ☐ goggles
10 ☐ other (specify _____)

23. WHICH OF THE FOLLOWING FIRST-AID MEASURES WERE INSTITUTED IMMEDIATELY? *(D150)*

1 ☐ none
2 ☐ change clothes
3 ☐ wash exposed area with soap and water
4 ☐ wash exposed area with other solvent
5 ☐ bath or shower
6 ☐ vomiting induced (method _____)
7 ☐ gave antidote (specify _____)

24. HOW MANY HOURS ELAPSED BETWEEN EXPOSURE AND BEGINNING OF COMPLAINTS?

(D160) __ __ hrs *(D161)* __ __ min

25. HOW MANY HOURS HAD COMPLAINTS BEEN APPARENT BEFORE MEDICAL ATTENTION RECEIVED?

(D170) __ __ hrs. *(D171)* __ __ min

25. WHAT COMPLAINTS (SYMPTOMS) OTHER THAN THOSE IN THE CHIEF COMPLAINT WERE ASSOCIATED WITH THIS ILLNESS? *(D180)*

00 ☐ none
01 ☐ malaise
02 ☐ fatigue
03 ☐ confusion
04 ☐ headache
05 ☐ nervousness
06 ☐ hyperirritability
07 ☐ light-headedness
08 ☐ fainting
09 ☐ dizziness
10 ☐ dermatitis
11 ☐ coma, unconsciousness
12 ☐ skin flushing
13 ☐ increased sweating
14 ☐ cyanosis
15 ☐ blurred vision
16 ☐ increased tearing
17 ☐ rhinitis
18 ☐ nasal stuffiness
19 ☐ increased salivation
20 ☐ tightness in chest
21 ☐ difficult breathing
22 ☐ palpitations
23 ☐ nausea
24 ☐ vomiting
25 ☐ abdominal pain, cramps
26 ☐ diarrhea
27 ☐ muscular weakness
28 ☐ tremor, fasciculations
29 ☐ convulsions
30 ☐ paresthesiae
31 ☐ other (specify _____)
32 ☐ fever

TREATMENT AND CLINICAL COURSE *(present illness)*

27. NAME OF ATTENDING PHYSICIAN

_____ MD

PHYSICIAN'S ADDRESS *(include zip code)*

29. NAME OF HOSPITAL

_____ No. days hospitalized *(D190)* __ __ __

30. TREATMENT

Treatment is presumed to include the usual supportive measures such as airway, oxygen, necessary IV fluids, etc. Hence these need not be mentioned unless their omission has contributed to the course. The medicine should include all pertinent ones, but single doses of aspirin, etc., may be omitted.

The physician need not detail each single dose as an individual listing. Rather, each change in schedule should be noted. The response should be either clinical or pharmacological and should be descriptive rather than a value judgment, for example.

EXAMPLE:

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
Atropine	1 4	0.8 mgm IV q min x 8	6.4 mgm	pulse, dilated pupils
Atropine	1 4	0.8 mgm IV q 1 hr x r	3.2 mgm	recovered consciousness
2-PAM	4 1	1 gm IV slowly	1000.0 mgm	no clinical,

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
(D200)	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	
	__ __		____.__ mgm	

31. OUTCOME:

(D210) 1 ☐ fatal 2 ☐ recovered 3 ☐ residual damage

32. FINAL DIAGNOSIS:

(D220) 1 ☐ pesticide intoxication 2 ☐ solvent intoxication 3 ☐ drug intoxication 4 ☐ other

33. CONFIRMATION OF ETIOLOGIC AGENT:

EXAMPLE

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
Parathion	8 / 0 4 / 2 9 0	Container	6	5000	ppm	EC
Parathion	8 / 0 4 / 2 9 0	Vomitus	1	500	ppm	U/V
PNP	0 / 0 7 / 4 7 8	Serum	2	2	ppm	Elliott
PNP	0 / 0 7 / 4 7 8	Urine	3	45	ppm	Elliott

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
(D230)	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	
	__/ __ __/ __ __ __ __		__		ppm	

34. HAS SUBJECT HAD A PREVIOUS EPISODE OF PESTICIDE POISONING? *(D240)* 1 ☐ yes 2 ☐ no 3 ☐ unknown
(if yes, give date, etc., below)

Dates (mo./yr.)	Has PHS 1.165-4, ACUTE EXPOSURE RECORD, been completed for each episode? Yes	No
(D241) __ __/ __ __	1 ☐	2 ☐
__ __/ __ __	1 ☐	2 ☐
__ __/ __ __	1 ☐	2 ☐
__ __/ __ __	1 ☐	2 ☐

***If PHS 1.165-4 has not been completed complete one now.**

35. WERE OTHER WORKERS OR FAMILY MEMBERS ALSO EXPOSED OR ILL? *(D250)* 1 ☐ Yes 2 ☐ No
How many? __ __ *(Give details below)*

36. CONCLUDING REMARKS: *(D260)* 1 ☐

L. L. Ramsey

Perhaps, it would be illuminating to look at major historical developments to see how we arrived at this point in pesticide regulation and then to conclude with a review of FDA's pesticide residue findings in food.

1906 - The Food and Drugs Act of 1906

The administration of this Act was lodged in the old Bureau of Chemistry of the U. S. Department of Agriculture. The Act contained no authority for establishing pesticide residue tolerances.

The Act required the Government to "establish that the added poisonous or deleterious substance may render the article injurious" before it could take action against a shipment of food bearing excessive pesticide residues.

1910 - Federal Insecticides Act of 1910

This Act covered only insecticides and fungicides and was intended to protect the farmer against adulterated and fraudulent products.

1927 - The regulatory functions of the Bureau of Chemistry were separated from the research functions and the Food, Drug, and Insecticide Administration was created to administer the Food and Drugs Act of 1906 and the Federal Insecticides Act of 1910.

1920 - 1939 - A period of zealous regulatory action against shipments of fruits and vegetables containing excessive residues of lead, arsenic, and fluoride, particularly during the 30's. The informal tolerances for spray residues on fresh fruits and vegetables had been reduced yearly until in 1932 they were set for arsenic at 1.4 ppm; lead, 3.5 ppm; fluoride, 2.8 ppm.

1938 - The Federal Food, Drug, and Cosmetic Act enacted

This Act contained the so-called poison *per se* rule: "Any poisonous or deleterious substance added to any food except where such substance is required in the production thereof .... shall be deemed to be unsafe ...." The law also provided authority for establishing safe tolerances for poisonous substances such as pesticides.

1940 - President Roosevelt's Reorganization Plan

The Food and Drug Administration was removed from the Department of Agriculture and placed in the new Federal Security Agency. The unit administering the Insecticides Act was left in the Department of Agriculture.

1940 - Informal tolerances on apples and pears were raised after a study by the Public Health Service as follows: arsenic, 3.5 ppm; lead, 7 ppm.

1944 - First legal tolerance established for a pesticide residue at 7 milligrams fluorine per kilogram on apples and pears.

1945 - Informal tolerance for DDT set at 7 ppm on apples and pears.

1946 - Court decision held the tolerance for fluorine to be null and void because the residue was actually cryolite, not fluorine.

1947 - The Federal Insecticide, Fungicide, and Rodenticide Act was enacted

This Act was designed to exercise more effective control over pesticides, particularly the new organic pesticides which were proliferating. The Act requires label registration of these pesticides moving in interstate commerce, the registration being based upon data showing that the pesticide is effective for the control of pests and safe when used in accordance with directions on the label.

1950 - The Delaney Committee hearings on pesticides and food additives.

1950 - FDA spray residue hearings with respect to fresh fruits and vegetables.

1954 - The Pesticide Chemicals Amendment (The Miller Amendment)

Established the present petition clearance procedure for setting tolerances for pesticide residues on raw agricultural commodities. This was the first pre-testing, pre-clearance procedure for chemical agents used on food. It shifted the burden of proof. The industry was required to show that the pesticide was safe before it was used instead of the Government being required to show that the pesticide was unsafe after it had been used.

1955 - Tolerances on fresh fruits and vegetables established for a long list of pesticides based on the 1950 spray residue hearings.

March 25, 1955 - Tolerances for residues of sesone established at 6 ppm on potatoes, peanuts, peanut hulls, peanut hay and at 2 ppm on asparagus and strawberries, the first tolerances under the Miller Amendment. Additional tolerances for other pesticides have followed to date.

1962 - Silent Spring by Rachel Carson contributed greatly to a general public awareness of the pesticide problem.

1963 - A Science Advisory Committee appointed by President Kennedy largely because of the furor created by Silent Spring issued a report entitled "The Use of Pesticides." The Committee recommended among other things that the concepts of zero tolerance and no-residue be reviewed, that the accretion of pesticide residues in the environment be reduced by orderly means, and that the elimination of persistent pesticides should be the goal.

1963 - Minute residues found in a wide variety of products because of the use of analytical methods based on gas liquid chromatography which have a sensitivity several magnitudes greater than the sensitivity of methods previously employed and provide means of finding metabolic products. Extensive regulatory action was taken against milk; cauliflower; dairy feed, such as alfalfa, corn silage, and dried sugar beet pulp; and other food crops.

October 13, 1963 - The actionable level for DDT residues in milk was reduced from 0.1 ppm to 0.05 ppm for DDT and for dieldrin and heptachlor epoxide it was set at 0.01 ppm and the states were notified.

May 1, 1964 - Interdepartmental Agreement

An agreement entered into voluntarily by the Departments of Agriculture, Health, Education, and Welfare, and Interior for the purpose of coordinating the activities of the three Departments pertaining to pesticides. This Agreement implemented one of the recommendations of the PSAC report of May 15, 1963.

April 13, 1966 - USDA and HEW published a joint statement of implementation of the report of an NAS-NRC "zero committee." Where there was any reasonable expectation of residue, however minute, the USDA would not grant a pesticide registration until the Food and Drug Administration had established a pesticide residue tolerance. The rather formidable task of converting a large number of label registrations by USDA based on no residue to label registrations based on a negligible residue tolerance got under way and still continues.

1967 - Tolerance established at 0.05 ppm for residues of DDT, TDE, and DDE singly or in combination in fluid milk pursuant to a report of a Scientific Advisory Committee dated October 26, 1966.

1968 - DDT tolerances lowered to levels no higher than necessary to cover residues incurred in good agricultural practice.

1969 - Tolerances for other pesticides reduced or proposed for reduction including captan, folpet, and TDE. Seizures of Coho salmon because of high levels of DDT.

In addition to the PSAC report of 1963, to which I alluded a few moments ago, there have been a number of other reports by nationally recognized advisory bodies. These reports are all directed toward a sound national policy on pesticides, and thus worthy of our consideration.

1. Ribicoff Report of July 21, 1966.

Senator Ribicoff served as the chairman of Senate Subcommittee.

The Report of this Subcommittee is well balanced. It recognizes the valuable role the newer chemical pesticides have played in the improvement of agricultural production and in the furtherance of public health and it recognizes the dangers to our overall environment as suggested in Miss Carson's popular book Silent Spring. In a section headed "The Benefit-Risk Equation" it is stated that "the committee found no reliable evidence to suggest that the benefit-risk equation was presently unbalanced in any significant way." However, the Report goes on to warn that more information is needed to guarantee future balance of the benefit-risk equation and to assure public confidence. This Report included a comprehensive series of recommendations.

2. Whitten Report, 1966.

Congressman Whitten served as the Chairman of a Subcommittee of the House. This report notes that the book Silent Spring by Rachel Carson influenced the concern of the public over the use of pesticides and points out the unwarranted implications in this book. In general, the report is not critical of the use of pesticides; no recommendations were made.

3. The NAS-NRC Report on Persistent Pesticides, May 1969.

In the preface the Committee refers to the PSAC Report of 1963 and notes that progress has been made but expresses concern about what remains to be done and about gaps in knowledge of pesticides. The Committee declares ".... there is an immediate need for world-wide attention to the problem of buildup of persistent pesticides in the total environment."

The principal recommendation of the report is "that further and more effective steps be taken to reduce the needless or inadvertent release of persistent pesticides into the environment."

4. HEW Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, November 1969.

November 1969 - HEW Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health.

While the Commission found itself in agreement with this rather broad and general recommendation of the NAS-NRC Committee on Persistent Pesticides, it concluded that the value of this recommendation would be considerably enhanced if it were made somewhat more specific and spelled out in greater detail. Toward this end, the Commission directed a number of specific recommendations carefully weighing the benefits of modern pesticide usage against the possible risks to man's health and the quality of his environment. In all, the Commission made 14 specific recommendations, but I believe that only three are of sufficient interest to this audience to be mentioned at this time.

III. Eliminate within two years all uses of DDT and DDD in the United States, excepting those uses essential to the preservation of human health and welfare and approved unanimously by the Secretaries of the Departments of HEW, Agriculture, and Interior.

IV. Restrict the usage of certain persistent pesticides in the United States to specific essential uses which create no known hazard to human health or to the quality of the environment and which are unanimously approved by the Secretaries of the Departments of HEW, Agriculture, and Interior.

V. Minimize human exposure to those pesticides considered to present a potential health hazard to man.

Besides these there have also been the reports of congressional hearings on specific aspects of our pesticide problem, such as the Fountain Committee hearings; all of these have exerted an influence on the pesticide policy of the Federal Government.

On December 2, 1970 the President's Reorganization Plan No. 3 became effective. This plan created the Environmental Protection Agency and transferred the responsibility for establishing tolerances for pesticide residues on raw agricultural commodities and processed food from the FDA to the new agency. FDA will continue with its pesticide tolerance enforcement program as well as its monitoring program for pesticide residues in food.

In conclusion, our over-all basic problem in the pesticide area is to decide what actions should be taken consistent with a policy that will keep the benefit-risk equation in balance, because the safety of any pesticide usage is not absolute regardless of the quantity of favorable data that may have been adduced. There is always some risk, be it ever so slight, and thus the benefits that may accrue from the usage of any pesticide must be weighed against the risk to be incurred.

SELECTED STUDIES ON PESTICIDES IN FISH AND WILDLIFE

Thomas W. Duke

Pesticides and possibly polychlorinated biphenyls (PCBs) are affecting our nation's fishery resources. Seafood products were seized on at least two occasions in 1969 because of high residues of pesticides[1] and oyster and clam beds on the eastern shore of Virginia were closed temporarily because of potential contamination from DDT.[2] Fortunately, the occurrence of high levels of pesticides in seafood organisms is rare, but low levels of these chemicals (lower than levels considered to be harmful to human health) and PCBs continue to appear in oysters, shrimp, fish, and other estuarine fishery organisms. Although these low levels are not considered to be harmful to human health, we do not yet know precisely how they affect the organisms in which they occur.

Much research effort is being devoted to determine the fate of pesticides and PCBs in the estuarine environment and the effect of these chemicals on estuarine organisms. Fate or occurrence is observed through monitoring programs whereby organisms, sediment, and water are collected and analyzed for the desired chemicals. Information obtained from the monitoring program is used to design laboratory experiments to determine effects of environmental levels of the chemicals on organisms. For example, investigators at our laboratory, in cooperation with National Marine Fisheries Service Laboratory (N.M.F.S.) at Galveston, Texas, examined a limited number of shrimp from Galveston Bay, Texas for chlorinated hydrocarbons on a quarterly basis in 1969 (1). They found DDT in hepatopancreatic tissue in samples taken in the summer. In laboratory experiments to test the effect of these environmental levels of DDT on shrimp, some test shrimp died of DDT poisoning. Since DDT was localized in the hepatopancreas of the shrimp from Galveston Bay and this organ is discarded when shrimp are prepared as seafood, these shrimp would have been satisfactory for human consumption according to existing regulations. However, if the residues were representative, the population was endangered at this particular time because of the effect of DDT on the shrimp. Fortunately, subsequent samples of shrimp from Galveston Bay contained little or no DDT.

Pesticides can reach estuaries through run-off from agricultural areas, direct application for noxious insects and municipal and industrial effluents, but PCBs are generally considered to be industrial pollutants. A correlation between application of DDT to farmland and occurrence of the chemical in oysters was shown (2). A similar correlation was evident when DDT was applied to beaches to control the stable fly. Instances of local pollution by industrial and municipal effluents also were recorded. No apparent correlation exists between pest control programs and occurrence of PCBs but at least one industrial source has been located (3). Although major sources of organochloride pesticides and PCBs may differ, their chemical structure and potential danger to estuarine organisms are similar.

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[1]Coho salmon from Lake Michigan
Canned mackerel from California

[2]National Fisherman, October 1970

Pesticides and PCBs can be classified according to their chemical structure. The chlorinated hydrocarbon pesticides such as DDT and its metabolites and dieldrin are persistent, insoluble in water but soluble in lipids whereas the organophosphates are less persistent and often hydrolyze in seawater. PCBs resemble DDT in structure and are chemically inert, non-volatile compounds. Aroclors® (Monsanto Company Trademark) are mixtures of PCBs that vary in position and number of chlorine atoms. Aroclor 1254 and 1260 (54 and 60 percent chlorine by weight) have appeared more often than other Aroclors in our monitoring samples. An excellent description of structural and physical properties of PCBs has been presented (4).

Pesticides entering an estuary can be concentrated through bioaccumulations, sorption to sediment particles and detritus and by chemical precipitation; conversely, these chemicals can be diluted and dispersed through mixing and transport with tidal currents, co-distillation, and emigration of animals that have accumulated the chemicals (Figure 1). Animals can accumulate and concentrate pesticides in their tissues and some animals serve as biogeochemical agents in the estuary. For example, shellfish can remove particulate matter from sea water and deposit the matter in pseudofeces and feces on bottom sediments. Mussels are important in the estuarine phosphate cycle as a depositional agent - extracting particulate phosphorus from sea water and making it available to deposit-feeders (5). Perhaps populations of shellfish could act in a similar manner with pesticides by filtering pesticide-laden particles from the water and depositing them on the bottom. This action would tend to conserve in the estuary pesticides that otherwise could be transported to sea. Pelagic animals, however, can transport pesticides out of the estuary as they emigrate. Croakers leaving Pensacola Bay, Florida, transported one-half pound of DDT and its metabolites from the bay to the Gulf of Mexico (2).

Fate and Effect of Pesticides

Results of various monitoring programs give us some indication of the fate of pesticides that reach the estuarine environment. Residues found as part of N.M.F.S.'s national monitoring program have been summarized and discussed (6). Levels of chlorinated pesticides in oysters and estuarine environment of the Mobile Bay, Alabama area have been reported (7) and also levels of chlorinated hydrocarbons in organisms from estuaries in California (8). Residues of pesticides in some estuarine fish over a 3-year period (9) and pesticide levels in fish of the Northeast Pacific (10) were recorded.

Recently, our laboratory participated in a cooperative monitoring study with N.M.F.S. laboratories in La Jolla, California and Seattle, Washington to determine residues of chlorinated hydrocarbons in certain commercial species that inhabit Pacific coastal and off-shore waters. Since we were interested in residues recently accumulated by the fish, livers were analyzed as indicator organs. The livers were prepared and analyzed by standard techniques used for tissue from other marine organisms (11). Residues of DDT and its metabolites in the liver of selected fish from the Pacific Ocean are presented in Table 1. Levels of these chemicals in the mackerel can be considered "background" and occur in many species analyzed at our laboratory. However, the lack of detectable amounts (<0.01 ppm) in salmon and the extremely high levels in rockfish are exceptional. The salmon were in the fifth-year class and had been out of fresh water for two or three years. Although residues were lacking in the liver, other tissues and organs, such as fat and ovaries, could have contained stored DDT. High levels of DDT in the bottom-feeding rockfish alert us to the need for further examination of this species and its environment.

Table 1.--Residues of DDT and Metabolites in Composite Samples of Fish Livers from Pacific Ocean[1]

	Date Collected m - d - y	Location	No. of Livers in Composite Sample	DDE	DDD	DDT	Total
				ug/kg (ppm) Wet Weight			
Sockeye Salmon (Oncorhynchus nerka)	2-23-70	49°16'N, 161°44'W	10	N.D.[2]	N.D.	N.D.	--
	2-27-70	51°30'-52°30'N 160°00'W	10	N.D.	N.D.	N.D.	--
	2-28-70	52°30'N, 160°00'W	10	N.D.	N.D.	N.D.	--
Jack Mackerel (Trachurus symmetricus)	5-7-69	31°25'N, 121°59'W	2	0.092	0.019	N.D.	0.11
	5-25-70	Cortez Bank	17	1.0	0.12	0.30	1.42
	5-27-70	6 mi. W. of Mission Beach Jetty, San Diego, California	10	2.5	0.16	0.41	3.07
Rockfish (Sebastodes miniatus)	5-13-70	Santa Monica Bay	10	141.	9.	12.	162.
(Sebastodes paucispinis)	5-13-70	Santa Monica Bay	9	510.	33.	48.	591.
(Sebastodes constellatus)	5-13-70	Santa Monica Bay	5	900.	56.	70.	1026.

[1]Salmon were collected and processed for analysis by personnel from National Marine Fisheries Service Laboratory, Seattle, Washington; Jack Mackerel and Rockfish, by National Marine Fisheries Service Laboratory, La Jolla, California. Analyses were performed at the Environmental Protection Agency, Gulf Breeze, Florida Laboratory under the supervision of A. J. Wilson, Jr., Chief Chemist.

[2]N. D. = Not detectable (< .01 ppm)

Table 2.--Accumulation of Aroclor 1254 by Estuarine Organisms (Jack I. Lowe, Unpublished Data)*

Animal	Size	Average Temp. (°C)	Average Salinity (‰)	Duration of Test (Days)	Concentration of Aroclor in Test Water (ppb)	Conc. in Living Animals (ppm)	Conc. Factors**	Mortality (%)
Oyster (Crassostrea virginica)	Adult (2 - 3")	9	28	14	5.0	26.0	5200	0
Shrimp (Penaeus duorarum)	Juvenile	19	31	20	5.0	33.0	6600	72
Fish (Spot) (Leiostomus xanthurus)	Juvenile (1-1/4")	9	28	21	5.0	120.0	24000	50
"	Juvenile (1-1/4")	15	27	19	5.0	46.0	9200	50
"	Juvenile (1-1/4")	15	27	28	1.0	17.0	17000	17

*Environmental Protection Agency, Gulf Breeze Laboratory, Gulf Breeze, Florida 32561

**$\frac{\text{Amount of Aroclor 1254 in animal (wet weight tissue)}}{\text{Amount of Aroclor 1254 in water}}$

Pesticides introduced into an estuary enter the biogeochemical cycles that are in operation within the estuary; therefore, we should evaluate the effect of these chemicals at the ecosystem and population level as well as the species level. Unfortunately, little information is available on the effect of pesticides on ecosystems. Observations were made on the effect of a herbicide, Dichlobenil, on the primary producers in a small (0.15 ha.) pond (12). About 1 month after treatment, the dominant hydrophytes in the pond suffered a definite decline. All of the Chara vulgaris and 80% of the Potamogeton pectinatus were eliminated. The number of blue-green algae increased as the hydrophytes were eliminated. The ecosystem regained its original balance of plants in about 4 months. A striking effect of environmental levels of DDT on a population of seatrout was reported recently (13). Residues of DDT in the yolk of speckled seatrout, Cynoscion nebulosus, were correlated with regional declines in productivity of this species. Recent data indicate that the fishery may be recovering from the pesticide stress. To my knowledge, this is the first documentation of the effect of environmental levels of pesticides on an estuarine fishery.

Pesticides entering the food web of an estuary can move from plants to animals to large animals as the organisms eat and are eaten. Green plants occupy the first trophic level; plant eaters or herbivores such as zooplankton, and some fish and mollusks occupy the second level; and carnivores such as large fish form the third and possibly a fourth.

Only a few selected research projects will be presented in the following discussion. Reviews are available in the literature pertaining to pesticides in the estuary (14), (15), (16).

Pesticides can affect the capacity of phytoplankton to photosynthesize and these minute plants can also transfer accumulated pesticides to herbivores. Studies of the effect of 17 toxicants on five species of algae showed the toxicity of DDT varies with the solvent used and 5 ppm lindane had no effect on any of the species tested (17). In another experiment, Chlorella sp. rapidly took up DDT labeled with carbon-14 (18) by absorption. Concentrations of DDT in the parts per billion range reduced photosynthesis in laboratory cultures of four species of coastal and oceanic algae (19). Laboratory experiments have shown partition coefficients (weight concentration factors) for DDT of 2.5×10^4 for Syracosphaera carterae and Thalassiosira fluviatilus and 8.0×10^4 for Amphidinium carteri (20). Investigations of the effects of sub-lethal concentrations of urea herbicides on the total protein, carbohydrate, chlorophyll, and carotenoid content of six genera of unicellular algae were conducted at this laboratory (21). Low levels of certain herbicides decreased growth of the algae and decreased carbohydrate content but produced no effect on protein content.

Brine shrimp (Artemia) and copepods are often used in laboratory experiments as representatives of the second trophic level. An example of the effect of DDT on the reproductive capacity of Artemia has been demonstrated (22). Second and fourth generation brine shrimp from populations treated with DDT in 1966 showed no reduction in reproductive performance. However, residual DDT killed some of the nauplii when they emerged. Grosch points out that this type of attrition would be very difficult to detect in nature. Evidently, Artemia also can accumulate DDT in their natural habitat. Other investigations showed residues of DDT in brine shrimp nauplii from California and Utah and the nauplii from Utah contained three times as much DDT as

those from California (23). Crabs fed nauplii from California had a good survival rate and showed no abnormalities, but crabs fed nauplii from Utah suffered marked mortality and some species exhibited abnormalities. These investigators suggested that the differences in normality and survival appeared to be related to the DDT content of the nauplii.

Filter-feeding mollusks can be affected by many of the pesticides in use today and some of those chemicals are particularly toxic to embryonic development and larvae. Acute toxicity data obtained with bioassay tests are helpful in illustrating the relative toxicity of these compounds to oysters. Laboratory studies on the effects of pesticides on embryonic development of clams and oysters and their larvae indicate the need to evaluate effects on all stages of the life cycle of an organism (24). Most of the pesticides tested affected embryonic development more than survival or growth of larvae; however, some reduced larval growth with little effect on embryonic development. Anomalies were found in larvae of bay mussel, Mytilus edulis, after these animals were exposed to 1.5 mg/liter of Sevin® (Union Carbide Company Trademark) for 48 hours (25). The need for studies of long-term exposures to sublethal concentrations of pesticides was demonstrated by investigators at this laboratory, who exposed oysters for 9 months to a mixture containing 1.0 ppb each of DDT, parathion, and toxaphene -- a mixture applied at different concentrations to agricultural crops in Northwest Florida (26). The test oysters suffered a loss in weight after 6 weeks exposure but the loss did not become significant until after 22 weeks had passed. After 9 months, histopathological examination of the oysters revealed considerable pathology that was apparently due to the pesticide.

Fish, as part of the third trophic level, have been much investigated for pesticide effects, often using death as a criterion for effects. Other criteria that could be used include behavior and enzyme activity. The capacity of sheepshead minnows, Cyprinodon variegatus, to avoid selected insecticides and herbicides has been investigated (27). Test fish avoided water containing DDT, endrin, dursban, and 2,4-D, but did not avoid test concentrations of malathion or Sevin. Hansen also is studying the effect of pesticides on the salinity preference of fish. Inhibition of acetylcholinesterase in brains of fish has been used to monitor organophosphorus pesticide pollution in estuarine waters (28). Organophosphorus compounds inhibit this enzyme which is essential to nerve function. Experiments also showed that specific levels of brain cholinesterase activity relate to extent of exposure and death of sheepshead minnows for several organophosphate pesticides (29). Thus, the enzyme can be used to detect these compounds and assess their threat to fish in the environment.

Fate and Effect of Polychlorinated Biphenyls

A series of "unknown" peaks appeared in 1966 in gas chromatograms analyzed for chlorinated hydrocarbons in wildlife. Similar peaks were later identified (30) as polychlorinated biphenyls. Since that time, PCBs have appeared in seals and porpoises in Scotland (31), birds and bird eggs in Britain (32), fish, mussels, and birds from the Netherlands (33), and from several estuarine areas in the United States (34). Fish and shellfish from Texas, Georgia, and South Carolina collected as part of BCF's national monitoring program also contained residues of these chemicals, including Aroclor 1260 (Butler, unpublished data).[3]

[3]P. A. Butler, Consultant, Environmental Protection Agency, 106 Matamoros Drive, Gulf Breeze, Florida 32561

Aroclor 1254, another of the series of PCB compounds, was found in the water, sediment, and biota of Escambia Bay, Florida (3).

Aroclor 1254 was widely distributed in the bay system. Only one source of the chemical, an industrial plant on the Escambia River was located, but the chemical occurs in sediment and in tissues of pelagic and sessile organisms that are widely distributed within the estuary. The widespread distribution is an indication of the extent of biological and physical transport of the chemical in the ecosystem.

Aroclor 1254 was first discovered in oysters in April 1969 and later appeared in water, sediment, fish, blue crabs, and shrimp. One source of the chemical, an industrial plant on the Escambia River, was located by analyzing 30 water samples from Escambia Bay and River. The Aroclor reportedly entered the plant's effluent through accidental leakage of a heat exchange fluid. Levels in the water near the plant decreased abruptly when the leakage was corrected.

Investigators from our laboratory cooperated with representatives from several State of Florida Agencies, the University of West Florida, and industry to locate and stop the leakage of the pollutant into the estuary. As in many other instances, this pollution abatement required a team of the scientific community.

Several bioassay tests conducted in our laboratory to determine the effects of Aroclor 1254 on selected estuarine organisms have shown that under laboratory conditions, this chemical can be toxic to estuarine organisms (Table 2). Other information on the toxicity of Aroclor 1254 at concentrations in the parts per billion range to laboratory animals has been reported (3), (35).

The potential hazard of PCBs in the environment has been recognized by the Monsanto Chemical Company. Officials of the company announced recently that sales of PCBs in the future would be limited to those who could control disposal of the final product. This should, we hope, reduce future introduction of PCBs into our ecosystem.

Future Responsibilities

We must continue to monitor estuaries to determine the occurrence of toxic materials and the effect of these materials on the biota. Such a need was illustrated in the Report of Committee on Persistent Pesticides, Division of Biology and Agriculture, National Research Council to U. S. Department of Agriculture (May 1969):

> "The Committee concludes that there is substantial evidence of continuing damage in some areas, particularly to fish and birds, by pesticide residues at present environmental levels. There are examples of concentrations in food chains at levels that are lethal to predators. Exposure to pesticides at sublethal levels probably produces more subtle effects, causing changes in the physiology, biochemistry, or behavior of animals that may be harmful to the population as a whole. Certain game fish accumulate pesticidal chemicals by storage in the body and in the fat-rich yolk of egges (sic); there may be no injury to adult fish, but lethal or harmful amounts are acquired by the newly hatched offspring when they absorb the egg yolk. Studies on two continents show that the reproductive success of certain birds of prey is impaired by DDT and its metabolites, which apparently act to reduce eggshell thickness and thus to increase premature breakage of the eggs."

I am cautiously optimistic about future uses of pesticides in relation to fishery resources. I express this feeling on the basis of efforts being made in research, ongoing programs for monitoring and regulating pesticide usage, industrial concern, and a growing public awareness of the impact of pesticides on our environment. We can be optimistic but not complacent.

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Occurrence and Significance of Pesticide Residues in Water[1]

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Man throughout the civilized world is rapidly coming to realize that environmental contamination, with its harmful ecological implications, is a matter to be taken seriously. I bring to your attention one facet of environmental contamination; namely, water pollution by pesticides. It is but another example of the adage that a good thing in the wrong place can be undesirable.

The Problem

Water pollution by pesticides became a problem in the 1940's concurrently with rapid advances in pest control made possible by the development of new synthetic toxicants. Many of these synthetics are remarkably lethal to aquatic forms of life. Farmers were startled at the sudden loss of fish in their ponds and streams following rains sufficient to cause runoff from treated cropland (Young and Nicholson, 1951). Aerial applications of DDT to control forest insects were quickly followed by losses of valuable sports fish and the aquatic insects upon which they fed (Hoffman and Drooz, 1953; George, 1959).

Today we still experience periodic losses, but we know considerably more than formerly about their causes and prevention. We know that sublethal quantities of pesticides, primarily chlorinated hydrocarbon insecticides, occur widely and frequently in our streams, lakes, and even in the sea. This occurrence is indirectly evident through the recovery of residues from the tissues of fish (Nicholson, 1967; Anon., 1963), and directly evident by chemical analysis of water. In an effort to determine the extent of pesticide pollution throughout the United States, Weaver *et al.* (1965) examined water samples in September 1964 from 56 rivers and 3 of the Great Lakes. Chlorinated hydrocarbon ininsecticides were found in 44 rivers and in Lake Michigan at Milwaukee at concentrations ranging from 0.002 to more than 0.118 μg/liter. Dieldrin was found in 39 rivers and Lake Michigan; DDT, or its metabolite DDE, was found in 25 rivers; and endrin was found in 22 rivers and Lake Michigan.

The two principal sources of water contamination by pesticides today are runoff from the land and discharges of industrial wastes. Other causes are (a) activities intended to control aquatic life (plants, fish, or insects), (b) carelessness and accidents.

Runoff from the Land

Consider first insecticide runoff from the land. In 1959 my laboratory undertook to follow the course of water pollution by insecticides in a single large agricultural watershed over a period of nearly seven years (Nicholson *et al.*, 1966). We selected a 400-square-mile cotton-growing area in northern Alabama in which cotton acreage varied annually from 13,000 to 16,000 acres. From 8 to 84% of this acreage was treated with insecticides each summer depending upon the degree of boll weevil and

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bollworm infestation. The quantity of technical grade insecticides used each year varied from 12,000 to 140,000 pounds. Toxaphene, DDT, and BHC accounted for 84–99% of all usage.

Water sampling was done nearly continuously at a municipal water treatment plant situated at the downstream end of the river basin. Thus, water samples represented drainage from the entire study area. We learned the following:

(a) Insecticides did run off the land. They entered the river from the watershed in general, rather than from a few favorably located cotton fields.

(b) Toxaphene, DDT and BHC were recovered in water samples in concentrations generally less than 1 μg/l. Highest mean recoveries were usually made during the summer, the season of application.

(c) Nearly all water samples contained insecticides year around during years of heaviest application. Toward the end of two years of minimal application (12,000 and 14,000 lbs., respectively), the frequency of negative water samples increased, indicating an improvement in river water quality with diminished insecticide usage.

(d) Toxaphene and BHC, first and third in poundage applied, were the most frequently found in water. DDT, which constituted 26–35% of the pesticides used, was recovered only during the fifth and sixth years of observation.

(e) DDT exhibited a marked affinity for sediment, and suspended sediment was the primary vehicle for its transport, thus accounting for its tendency to appear less frequently in water. Toxaphene and BHC, in contrast, were found much less frequently in association with sediment and were transported primarily in solution in the water.

A study by Bailey and Hannum (1967) reported from California sheds further light on runoff as a means of pesticide transport. Approximately 20% of all pesticides used in the United States annually is applied in California. The areas studied included the agriculturally important Imperial, San Joaquin, and Sacramento Valleys, where irrigation is required for successful farming.

Major findings were:

(a) DDT, DDD, toxaphene, heptachlor epoxide, lindane, dieldrin, and BHC were found both in surface water and in tile drainage water in concentrations generally less than 1 μg/l.

(b) All aforementioned insecticides, except BHC, were found in sediment and ranged from 1 to 1200 μg/l.

(c) Thiophosphate insecticides, which degrade more readily, were detected primarily in agricultural drainage, irrigation wastewater, and surface water directly associated with insecticide applications.

(d) Pesticide concentrations were highest in agriculturally developed areas and decrease in surface water in proportion to inflow dilution and uptake by sediment and aquatic organisms.

Manufacturing Wastes

Manufacturing wastes also may contain quantities of pesticides sufficient to have a decided impact on water quality. The types of industries involved include producers of basic pesticides, cooperage firms that reclaim used pesticide drums, and textile plants that mothproof woolen yarns and fabrics with dieldrin. These plants usually have liquid wastes requiring disposal—wastes which frequently contain residues of unrecovered pesticides.

Virtually all of these industrial plants provide some sort of waste treatment, but it is not always as effective as it should be. Dilution in the receiving stream can-

not be depended upon to eliminate the impact of the waste load. Sublethal residues of chlorinated hydrocarbon insecticides can undergo a buildup in biotic components of the receiving water body, and ordinarily sublethal quantities of organophosphate pesticides may, through extended exposure, progressively inhibit the acetylcholinesterase enzyme to a degree that can kill aquatic life. Direct and catastrophic damage also has occurred when in-plant trouble resulted in an unanticipated slug discharge of wastes containing concentrations of a pesticide sufficient to be acutely toxic. An example of such a situation and its successful management follows.

A plant in Alabama which manufactures parathion and methyl parathion experienced a breakdown in its waste treatment facility in May 1961 (Anon., 1961). Process wastes were discharged to the sewerage system of an adjacent city and approximately 60% of the combined sewage and industrial waste was diverted, untreated, to a small stream during the breakdown. Fish, turtles, and snakes died along 28 miles of the stream, the average discharge of which at the time was 211 million gallons a day at a velocity of three-fourths mile per hour. The creek entered the Coosa River the average discharge of which was then about 28 times greater than that of the creek. Yet even with that dilution, parathion residues were recovered 90 miles down the Coosa and some lesser fish kills occurred in it. After a second fish kill in 1966, the company constructed a basin for temporary containment of its wastes, should another emergency arise. This simple device, along with the usually adequate waste treatment normally provided, should effectively prevent recurrence of the problems previously experienced.

Accidents and Carelessness

Perhaps the third most significant cause of pesticide pollution lies in accidents and accident's handmaiden, carelessness. Intensive educational campaigns sponsored by agricultural, conservation, water-pollution-control, and public health agencies and by the agricultural chemicals manufacturing industry have reduced the frequency of such occurrences. Most farmers have learned that it is inadvisable to dump unused spray residue where it might run into a waterway, and that they should not wash out spray equipment in a creek. Aerial applicators now pay heed to the protection of ponds and rivers. Nevertheless, some instances of water pollution by pesticides still occur as a result of thoughtlessness and accidents. An instance in which human health was at stake will serve as an example (Anon., 1964).

In 1964 a rancher instructed his hired hand to dispose of approximately fifty 4-lb. bags of over-age 15% parathion dust. Unknown to the rancher, this was done by dumping the bags off a highway bridge into the Peace River one mile upstream from the municipal water intake of Arcadia, Florida, a town of about 6,000 people. The act was discovered when some boys fishing near the bridge hooked a bag and had the foresight to report it.

The town fortunately had an auxiliary well for emergency use and immediately reverted to it. The citizens were instructed not to use the water, and flushing of the mains was begun. Subsequent analysis of water samples showed that the parathion concentration in the distribution system after flushing was generally less than 1 $\mu g/l$. However, a series of samples taken from a tap at the local bus station contained amounts up to 380 $\mu g/l$.

Investigation revealed that the bags of parathion had been dumped in the river about 10 days before their discovery. The bags were polyethylene lined and resisted rapid disintegration. Many were recovered unbroken and those that did disintegrate apparently did so intermittently over a period of several weeks. This may have been the reason that residue levels sufficiently high to be a threat to human health or the fish in the river did not occur. All but 8–12 bags were eventually found. Parathion residue occurred in river water

for about two weeks after discovery at concentrations generally less than 1 μg/l.

Control of Aquatic Life

The chemical control of aquatic weeds, rough fish, and aquatic insect pests is generally managed by professionals so that undesirable consequences are minimized. A need currently exists for herbicides approved for broader use in water. A joint committee of the Departments of the Interior and Agriculture are seeking a solution to this need. A similar, but remotely related, source of pesticide residues is poaching for fish. We still have instances where insecticides, frequently toxaphene or DDT, are illegally released in water to catch fish.

Ground Water Pollution

No broad discussion of this subject would be complete without considering ground water. The potential for pesticide contamination of ground water is very much less than for surface water. However, it can occur.

A case is on record in Florida where the municipal water supply wells of a city of 25,000 contained low levels of parathion (usually less than 1 μg/l) over a several month period in 1962-63. The city's water supply consisted of both surface water, which reached the municipal water treatment plant via a canal from a citrus fruit producing area, and of five wells which were located in the vicinity of the treatment plant. The water from both sources contained parathion. The wells were rather shallow—drilled to a depth of about 100 feet and screened both at the bottom and at about the 30- to 50-foot levels. It is speculated that heavy pumping from the wells drew down surface water from the canal.

A more serious instance occurred in the South Platte River Basin near Denver, Colorado in the mid-1950's, caused by seepage of 2,4-D and related compounds from an industrial waste lagoon (Cottam, 1960). Water from wells in a 6.5-square-mile area when used for irrigation was sufficiently contaminated to cause crop damage.

Eye (1968) concluded after a study of the physical-chemical behavior of dieldrin in the soil that residues of this insecticide cannot be transported in significant amounts through soils into subsurface water by infiltration, and therefore they pose no threat to the quality of ground water. We have examined many well water samples from the Southeastern States and only in a few instances have we detected any evidence of chlorinated hydrocarbon insecticides. In those few cases, I recall only two in which direct contamination did not seem to be a possible cause. On the other hand, Bailey and Hannum (1967) in California reported recovering a broad range of chlorinated hydrocarbon insecticides. ~~In those few cases I recall~~ FROM underground tile drains from irrigated cropland. They did not speculate on how insecticides entered the drains. A possible route might be through cracks or other direct passages from the surface.

In several of our mid-western States, where water of high quality is in limited supply, consideration is being given to using runoff water collected seasonally in playa lakes as a source from which to recharge ground water aquifers. The Robert S. Kerr Water Research Center of the Federal Water Pollution Control Administration at Ada, Oklahoma, is engaged in studies to determine the quality of recharged water, including the persistence and distribution of pesticides that may be contained in such water, after being pumped into the ground for storage.

Significance

We have seen that water contamination by pesticides occurs widely and commonly at concentrations generally less than 1 μg/l. Higher concentrations occur intermittently. But of what significance are such occurrences?

Aquatic Life

Quite clearly the unintentional killing of fish and other aquatic life by overwhelmingly lethal concentrations of pesticides is harmful and undesirable. Occurrences of this type are generally local, readily apparent, and sporadic, with partial or total repopulation quickly occurring.

Widespread, long-term, low-level contamination of the environment is much more difficult to evaluate and is a matter of growing public concern. It is caused primarily by a few compounds, members of the chlorinated hydrocarbon insecticide group—the so-called "hard" insecticides—that persist so long in nature and therefore escape our control after they are applied. Other pesticides, by and large, either degrade with reasonable rapidity or are so restricted in usage as to be of less concern except in special cases. One is tempted to speculate as to whether we would have had the public outcry over pesticides that we have experienced during the past 10 to 15 years had it not been for these few "hard" insecticides. I am inclined to think that it would have been much less extensive.

The single sublethal manifestation with chlorinated hydrocarbons that is most obvious, and the significance of which is least understood, is that of biological accumulation. Biological accumulation may occur through direct absorption from the water or by absorption and passage through the food chain. The implications for damage are great, but well defined examples of proved harm are few, perhaps because biological accumulation is not as generally damaging as feared, but also perhaps because the ecological relationships involved are so extremely complex that they are difficult to unravel.

Light has been cast on this phenomenon by numerous researchers. Cope (1965), investigating the distribution of DDT through various compartments of a simplified ecosystem, reported that two weeks after the application of ^{14}C–DDT at a concentration of 20 μg/l to aquarium water, the water contained 0.42 μg/l, soil contained 6 μg/kg, and vegetation contained 15,600 μg/kg. Two weeks after fish were placed into the aquaria, they contained 1,000 μg/kg of DDT. Woodwell *et al.* (1967) investigated biological concentration of DDT among various trophic levels of a Long Island salt marsh and reported values increasing from 0.04 mg/kg in plankton to 75 mg/kg in ring-billed gulls. Highest concentrations occurred in scavenging and carnivorous fish and birds, although the birds had 10–100 times more than the fish. Gakstatter and Weiss (1967) exposed bluegills and goldfish in aquaria to ^{14}C–DDT, dieldrin, and lindane to study uptake, retention, and release by the fish. They showed that the lindane was entirely released within two days and that more than 90% of the initial dieldrin was eliminated within two weeks. However, more than 50% of the DDT was still retained after 32 days. More significant, they showed that DDT and dieldrin were readily transferred from contaminated to uncontaminated fish held in clean water. Apparently, some of the persistent insecticides are capable not only of undergoing biological magnification but also of cycling between water and the organisms living in it.

The accumulation of pesticides in the bodies of fish has been cited as the probable cause of the secondary poisoning of a variety of fish-eating birds. The most notable example is that described by Hunt and Bischoff (1960) in which western grebes overwintering on Clear Lake, California died, presumably from eating fish containing high DDD residues. Keith (1966) reported an unusually high mortality of fish-eating birds between 1960 and 1962 at the Tule Lake National Wildlife Refuge in California, which he attributed, circumstantially, to ingestion of toxaphene accumulated in fish. A study of this refuge in 1965–66 (Godsil and Johnson, 1968), when endrin was the principal insecticide used on the nearby irrigated farmland, indicated a marked increase of endrin in

all trophic levels during the crop-growing season (May-Sept.) with a subsequent decline to near or below detectable limits in the off season. Fish accumulated maxima of 97 μg/kg in 1965 and 107 μg/kg in 1966. Endrin was not established as a permanent residue, and no wildlife losses were recorded. It is apparent that the so-called "hard" insecticides are not equally accumulative or persistent in food chain compartments.

Butler (1966 a, b, c) has done extensive work on the effects of low levels of chlorinated hydrocarbon insecticides on organisms of the marine environment. He showed that DDT in the water at levels as low as 1 μg/l caused a 20% reduction in oyster growth, and that oysters are efficient concentrators of DDT in their tissues. He believes that pesticides may be the cause of ill-defined but significant mortality, loss of production, and perhaps changes in the direction of natural selection in estuarine fauna. Cope (1965) concluded that exposure to sublethal amounts of DDT increases fish mortality by reducing resistance to other stresses.

Burdick and his co-workers (1964) in New York demonstrated that lethal amounts of DDT can be transmitted from female lake trout to their offspring through the egg. Lethality bore no relation to the concentration of DDT in the female. Fry died when the final contents of the yolk sacs were absorbed. These deaths occurred when the eggs contained DDT equivalent to 2.9 mg/kg or more of fry. This situation came to light when complete loss of lake trout fry occurred in 1955 and 1956 at a Lake George fish hatchery. It is a most subtle adverse effect that would be detected only under hatchery or laboratory conditions.

The influence upon the survival of aquatic organisms of transovarially conveyed pesticide residues is a subject worthy of further research. The period of dependence upon food stored in the egg sac may be for numerous fish species the most vulnerable period in their life histories as far as pesticides are concerned. If this is true, the chances are very slight that population losses would be directly observed in nature short of virtual elimination of a major species.

Much has been written about the effects of long-term exposure of aquatic organisms to pesticides at sublethal levels, but we still have a remarkably small amount of compellingly positive information indicating danger from organic chlorinated insecticides. DDT has received by far the most attention, possibly because its residues are so universally distributed. We need more research on other persistent insecticides. Although we do not have agreement within the scientific community concerning the danger of persistent residues in living organisms and in the environment, perhaps all can agree that it would be better if we did not have these uncontrolled residues.

Other Water Uses

In April 1968 the National Technical Advisory Committee on Water Quality Criteria of the Federal Water Pollution Control Administration submitted its first report to the Secretary of the Interior (Anon., 1968). This volume constitutes the most comprehensive document to date on water quality requirements for various uses. It contains recommendations for permissible limits for some pesticides.

The Subcommittee on Public Water Supplies based its recommendations on pesticides upon recommendations submitted by the Public Health Service Advisory Committee on Use of the Public Health Service Drinking Water Standards. The values were derived for that committee by an expert group of toxicologists and were established at those levels which, if ingested over extensive periods, could not cause harmful or adverse physiological changes in man. In the case of aldrin, heptachlor, chlordane, and parathion the values were set even lower than those physiologically safe, to avoid levels that could be tasted or smelled. Table 1 contains these recommendations.

Table 1. Surface Water Criteria for Pesticides in Public Water supplies (mg/l).[1]

	Permissible criteria	Desirable criteria
Aldrin	0.017	Absent
Chlordane	0.003	"
DDT	0.042	"
Dieldrin	0.017	"
Endrin	0.001	"
Heptachlor	0.018	"
Heptachlor epoxide	0.018	"
Lindane	0.056	"
Methoxychlor	0.035	"
Organic phosphates plus carbamates	0.1[2]	"
Toxaphene	0.005	"
2,4-D plus 2,4,5-T, plus 2,4,5-TP	0.1	"

[1] Adapted from Water Quality Criteria, Report of the National Technical Advisory Committee to the Secretary of the Interior, April 1968. Washington, D. C.

[2] As parathion in cholinesterase inhibition. It may be necessary to resort to even lower concentrations for some compounds or mixtures.

The subcommittees concerned with criteria for aquatic and wildlife (both freshwater and marine) and for agriculture each considered pesticides. The criteria, or formulae for determining criteria values, are generally too complex to justify discussion here, and the reader is referred to the original source.

An alternative suggestion for a water-quality criterion for fish, based on a group effect of about 100 organophosphorus and carbamate compounds, was derived at the Southeast Water Laboratory (Nicholson, 1967). This practical suggestion was based upon the ability of these compounds to inhibit acetyl-cholinesterase activity in the brains of fish. The degree of inhibition is a function of the compound, its concentration in water, and the duration of exposure. Death results from inhibition ranging from 40 to 70%. As little as 10% inhibition can be measured and statistically confirmed in a group of ten fish of the same species and of similar size. Therefore, it was suggested that 10% acetylcholinesterase inhibition in fish brain would serve as a good criterion of water quality involving chemicals capable of causing this inhibition. Unfortunately, no group effect for organochlorine insecticides has yet been developed upon which a similar criterion can be established.

Pesticide Pollution Control

The Southeast Water Laboratory has national responsibility within the Federal Water Pollution Control Administration for research leading to the control of pesticide pollution. Control is generally easiest at point sources; i.e., at industrial sources where waste effluent is discharged to a stream at a single outfall. We are currently beginning an inventory of waste-treatment practices at pesticide manufacturing and pesticide using industrial plants to establish a mutually beneficial relationship with some of these industries. Control may be accomplished by a variety of waste-treatment processes and by in-plant process changes. Effective control may be as simple as the provision of facilities for biochemical oxidation of effluents with auxiliary provision of a basin for containing extraordinary peak loads of wastes for more leisurely disposal. Our Laboratory is equipped with a variety of advanced analytical instruments, including a 100-megacycle high-resolution nuclear magnetic resonance spectrometer and a computerized mass spectrometer, with which we are able to determine the chemical nature of industrial waste effluents and assist in optimizing the design of advanced waste treatment systems.

The control of pesticide pollution associated with rural runoff is much more difficult to accomplish because its entrance into watercourses is not localized. Therefore, control must be accomplished by other means and ultimately rests in the hands of the users. Land-management practices designed to retard water runoff and soil erosion certainly are helpful measures. The retention of an untreated buffer strip adjacent to mountain streams was shown to prevent the runoff of DDT ap-

plied for forest insect control (Grzenda *et al.*, 1964).

We are conducting research with pure clay mineral model soils to develop basic concepts relative to the retention of representative pesticides on the land or their failure to be retained. Recently our scientists, cooperating with associates at Purdue University, demonstrated that s-triazine herbicides may be irreversibly adsorbed onto montmorillonite clay, and in so doing, undergo a chemical change to an innocuous compound (Russell *et al.*, 1968). Basic concepts developed are later confirmed with natural soils. The results frequently are directly applicable to rural runoff control recommendations.

Pesticide runoff from the land is directly related to runoff losses of both water and surface soil; they serve to transport pesticides from farm or forest to watercourses. Controlling this process are climatic, edaphic, hydrologic, physiographic, and cultural factors. If we knew more about the interplay of soil type, slope of the land, rainfall, and other climatic factors, cropping practices, and the behavior of the pesticides in use, we should be able to recommend measures to reduce the importance of rural runoff as a source of water pollution by pesticides. These recommendations might simply concern which pesticides to use or not to use in a given combination of circumstances. It might develop into water-pollution-control recommendations for geographic zones.

A comparable development has already been made in agriculture. I refer to the universal soil-loss equation that is applicable to guiding conservation farm planning throughout the United States (Wischmeier *et al.*, 1958; Wischmeier, 1969; Wischmeier and Smith, 1960, 1965). The factors upon which this equation is based are rainfall, soil-erodibility, slope length and gradient, cropping management, and erosion control practices. The possibility of extending the universal soil-loss equation and applying it to the prediction and control of pesticide pollution associated with rural runoff seems good and is being explored.

In the meantime, socio-economic developments are occurring outside the field of water pollution control that tend toward reduction of the water pollutional impact of the persistent organochlorine insecticides. The development of resistance to insecticides among cotton, corn, and sugarcane pests, to name a few, has forced total or partial abandonment of the formerly preferred "hard" insecticides in favor of more effective and, incidentally, less persistent types. Food and Drug Administration-controlled tolerance levels have required other changes. There is a growing public interest in environmental contamination control that may bring forth legislation outlawing the use of the "hard" insecticides as "hard" detergents were outlawed a few years ago. I should not like to see this happen, but would prefer to see substitutes used whenever it is feasible to do so, retaining the troublesome insecticides for use where they are absolutely necessary and where their usage will not result in further environmental contamination.

It is the responsibility of entomologists and leaders in the field of pesticide usage to take note, to look beyond the immediate problem of controlling insects, and to assume greater responsibility for preventing undesirable side effects resulting from the use of pesticides.

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PESTICIDE PROBLEMS IN WATER HYGIENE AND THEIR CORRECTION

Frederick C. Kopfler

A. GUIDELINES FOR PESTICIDES IN DRINKING WATER

The Water Supply Programs Division of the Office of Water Programs is responsible for recommending standards, limits and guidelines for a wide variety of chemical and biological contaminants of drinking water. Pesticides are among the chemicals for which limits have been recommended. The list of pesticides and the respective concentration limits of each are shown in Table I. These guidelines were formulated on the basis of fish toxicity data that were available. New standards have been proposed and are under consideration at this time. The proposed standards include additional compounds and list maximum allowable concentrations for both short term and chronic exposure. The proposed allowable concentrations for chronic exposure are generally higher than those of the present guidelines, but they are derived from animal and human toxicity data.

TABLE I

RECOMMENDED LIMITS FOR PESTICIDES IN DRINKING WATER

PESTICIDE	MAXIMUM PERMISSIBLE CONCENTRATION, mg/LITER[a]
Endrin	0.001
Aldrin	0.017
Dieldrin	0.017
Lindane	0.056
Toxaphene	0.005
Heptachlor	0.018
Heptachlor epoxide	0.018
DDT	0.042
Chlordane	0.003
Methoxychlor	0.035
Total organophorsphorous and carbamate compounds[b]	0.1
2,4,5-TP, 2,4,5-T, 2,4-D[c]	Individual limits = 0.1 mg/liter; Sum of any combination of chlorinated phenoxy aklyl pesticides = 0.1 mg/liter

[a]For long term exposure.

[b]Expressed in terms of parathion equivalent cholinesterase inhibition.

[c]Short period limit only: 2 to 3 days, no more than once or twice a year.

The thirteenth edition of Standard Methods for the Examination of Water and Wastewater includes a tentative gas chromatographic method for the determination of chlorinated hydrocarbon pesticides. Methods for the determination of organophosphorous and

Very little, if any, information is available concerning the quality of the water consumed by individuals and families not served by public or community water sources. A systematic survey of individual water supplies was conducted in four widely separated counties in Georgia. One of the objectives of the project was to examine a representative number of types of these supplies for pesticides as in the community water supply study. The 78 samples that were taken represented dug wells, bored, jetted, and driven wells, springs and cisterns. Table III summarizes this data. Two interesting comparisons between this data and that of the community supplies is that DDT was detected in more than 60% of these supplies as compared to 46.4% of the community supplies. While only 3.5% of the community supplies contained a residue at a concentration $\geq$ 0.1 ppb the figure for the individual supplies is 9%.

TABLE III

FREQUENCY OF OCCURRENCE OF INDIVIDUAL PESTICIDES IN INDIVIDUAL WATER SUPPLY STUDY

PESTICIDES	NO. OF TIMES DETECTED	% SAMPLES POSITIVE	MAXIMUM VALUE ppb	NO. OF SAMPLES > 0.1 ppb
pp'DDT	48	61.5	0.5	0.2, 0.3, 0.5
Dieldrin	5	6.4	<0.1	
Endrin	4	5.1	0.2	1 @ 0.2
Lindane	2	2.6	0.9	1 @ 0.9
Chlordane	2	2.6	<0.1	
Heptachlor	2	2.6	0.2	1 @ 0.2
Heptachlor-epoxide	1	1.3	0.2	1 @ 0.2
Aldrin	0	0	-	-

Table IV is a comparison of the distribution of pesticides in the community water supplies and the distribution in the individual supplies. It can be seen that about 10% fewer of the individual supplies were free of detectable residues. In the community water supplies, pp'-DDT was the residue that accounted for 80% of those samples containing one pesticide; the comparable value was 52% for the individual supplies.

TABLE IV

DISTRIBUTION OF RESIDUES IN THE WATER SUPPLY STUDIES

NUMBER RESIDUES DETECTED	COMMUNITY WATER SUPPLY STUDY		INDIVIDUAL WATER SUPPLY STUDY	
	Number	%	Number	%
0	72	42.4	25	32.0
1	56	32.9	46	59.0
2	18	10.6	4	5.1
3	13	7.6	2	2.5
4	8	4.7	1	1.3
5 & 6	3	1.8	0	0

carbamate compounds are currently being evaluated. Methods for the determination of the herbicides are available and should be evaluated before the fourteenth edition of Standards Methods is published.

B. SURVEYS OF PESTICIDES IN DRINKING WATERS

In 1969, the Bureau of Water Hygiene of the U. S. Public Health Service conducted a Community Water Supply Study (CWSS) to determine if the American consumer's drinking water met the Drinking Water Standards. This study was designed to give an assessment of drinking water quality, water supply systems and surveillance programs in urban and suburban areas in each of the nine regions of the Department of Health, Education, and Welfare. These areas were selected to give examples of the several types of water supplies in the country.

A whole Standard Metropolitan Statistical Area (SMSA) was the basis of each study, except in Region I where the entire State of Vermont was included, with evaluations made on all public water supply systems in each study area. This coverage allowed an assessment of the drinking water quality of the large central city, the suburbs, and the smaller communities located in the counties in the SMSA, and the interaction between them.

Table II summarizes the pesticide data obtained from the analysis of 170 samples during the CWSS.

TABLE II

FREQUENCY OF OCCURRENCE OF INDIVIDUAL PESTICIDES IN CWSS

PESTICIDES	NO. OF TIMES DETECTED	% SAMPLES POSITIVE	MAXIMUM VALUE ppb	NO. OF SAMPLES > 0.1 ppb
pp'DDT	79	46.4	<0.1	0
Endrin	26	15.3	<0.1	0
Dieldrin	17	10.0	0.1	1 @ 0.1
Lindane	16	9.4	0.2	2 @ 0.2
Chlordane	13	7.6	0.2	1 @ 0.2
Heptachlor	11	6.5	0.2	2 @ 0.2
Heptachlor-epoxide	10	5.9	<0.1	0
Aldrin	7	4.1	<0.1	0

Only six samples or 3.5% of the total contained a residue at a concentration equal to or exceeding the reporting limit of 0.1 ppb. DDT was detected in almost 50% of the supplies. Aldrin was found in 7 supplies. It was determined that six of these were ground waters while one was a surface supply and it also contained four other residues. Toxaphene and methoxychlor were not detected.

A similar evaluation of water supplies was conducted in Tennessee in late summer of 1970. Twenty-six samples were analyzed for chlorinated pesticides; one contained 0.1 ppb chlordane, two contained <0.1 ppb pp'-DDT and the no residues were detected in the remaining 23.

In addition to these special studies, the Division is responsible for the on going surveillance of Interstate Carrier Water Supplies. There are 710 such water supplies and each must be examined at least once every three years. Only trace amounts of chlorinated pesticides have been detected in samples submitted for analysis in conjunction with this program.

The growing national attention to the use of 2,4,5-T has brought up the question as to whether this herbicide is getting into drinking water supplies where it may constitute a potential hazard to those who consume the water. There is very little information available at the present time to provide a basis for answering this question because monitoring of public water supplies in the United States for 2,4,5-T and related herbicides has been limited. It is generally recognized, however, that the contamination of drinking water supplies represents a potentially significant route for exposure of human beings to this material especially in those areas of the country where there is direct application of the herbicide to water for weed control and to a lesser extent where there is runoff from forested areas treated for brush control.

In the evaluation of public drinking water supplies the present maximum permissible concentration is 0.1 mg/liter (ppm) for either 2,4,5-T or the sum of any combination of 2,4,5-T and other related compounds as was shown in Table I. A survey was planned so that the results could be assessed in relation to this guideline in the future consideration of an ultimate standard for 2,4,5-T and other related herbicide in drinking water.

This survey was conducted during August through November 1970. Table V is a summary of the results of this survey.

TABLE V

OCCURRENCE OF PHENOXY ACID HERBICIDES IN 58 WATER SUPPLIES

HERBICIDE	WATER SUPPLIES IN WHICH HERBICIDE DETECTED		CONCENTRATION (ppb)		
	Number	Percent	Low	Medium	High
2,4,5-T	11	19.0	<0.5	<0.5	0.57
2,4-D	18	31.0	<0.5	<0.5	3.44
2,4,5-TP	4	6.9	<0.5	<0.5	<0.5

Analyses of the data obtained from this one-time sampling of community water supplies, which followed generally the period of seasonal use of 2,4,5-T and related herbicides, indicate that only traces of these herbicides could be detected in up to 19 to 31 percent of the water supplies. These trace amounts of 2,4,5-T and related herbicides, generally at concentrations less than 0.5 ppb and ranging up to 0.57 ppb for 2,4,5-T and 3.44 ppb for 2,4-D in the raw and/or finished waters, are extremely low when compared to the present Public Health Service guideline of a maximum permissible concentration of 0.1 mg/liter (ppm) for either the individual herbicide or the sum of any combination of these herbicides.

On the other hand, the survey substantiated the unquestionable fact that the use of

2,4,5-T and related herbicides on watershed areas and water supply sources results in the occurrence of the herbicides in the raw and/or finished waters of community water supplies. The lack of occurrence or the detection of 2,4,5-T and related herbicides at very low concentrations or in trace amounts in community water supplies in this survey could possibly be the source of a false sense of security from the public health standpoint.

The results of these surveys of drinking waters indicate that contamination of a water supply with a chlorinated pesticide in excess of values in Table I would be an exception rather than the rule. However, the water systems in many metropolitan areas are presently faced with several problems relative to the use of pesticides, insecticides, and herbicides. This includes their use by homeowners on lawns and around the foundation of their homes to control termites, by the farmers for agricultural control, and by utilities, highway departments, and local governments for controlling growth along right of ways.

C. INVESTIGATION OF A PRIVATE WELL

The use of pesticides and insecticides on lawns and for termite control is a concern of public health officials. All the substances tested during the CWSS have been and are being used for termite control. They are the so called hard pesticides, such as chlordane, dieldrin, endrin, aldrin, toxaphene heptachlor, lindane, and DDT, which remain in the soil for six months to as much as seven years. In providing protection for a house, the exterminator jets a solution about eight feet into the ground all around the foundation and in the basement floor. The number of injections and amount of substance depends upon the size, shape, and other characteristics of the house. In the past chlordane was most widely used; however, dieldrin now seems to be more effective and to last longer. Registration of aldrin, dieldrin and mirex for all uses were cancelled last year but they may still be in use.

The soft substances which breakdown faster require more frequent reapplications than the hard. It is quite apparent that further study is necessary to determine which procedure should be used, hard agents with less frequent application or soft with more frequent applications, to insure that the potential hazard to public and private wells is eliminated.

During the Community Water Supply Study, the Suffolk County, New York Department of Health staff investigated a private well supplying a house that had recently been treated for termites. A solution was used containing approximately 10,000 ppm of chlordane. It had been injected into the ground around the foundation and through the cellar floor. It was also sprayed on the wood just above the foundation. Based upon a noticeable change in the taste of the water, the county requested that the Bureau of Water Hygiene run the series of pesticide tests that were being performed for the CWSS.

Of the ten pesticides for which the sample was tested, three were found in trace amounts similar to that found in public supplies: dieldrin, <0.1; heptachlor, 0.2; and heptachlor-epoxide, 0.1 ppb. However, 12.9 ppb of chlordane were found. This is over four times the limit of 3 ppb. The owner of the contaminated private well, at the request of the county staff, pumped his well fairly constantly over a five to six week period. A second sample was taken and also forwarded to the Gulf Coast Water Hygiene Laboratory for analysis. The tests on this sample showed 1.5 ppb of chlordane with none of the other substances being detected.

Although there was an old uncapped well nearby which might have been partially responsible, the fact that the well was only three feet from the house foundation would seem to indicate a problem regardless of the old well. Many of the older houses in that county have their wells close to house foundations or in the basement. Presently the county sanitary codes require only a three foot space between the house foundation and its well. In view of these facts, it is hard to imagine such wells as not becoming contaminated.

The foregoing, although based on a private well case, clearly indicates need in several areas. A complete investigation should be made as to the entrance of pesticides into ground water, their persistance, and their rate and distance of travel. Such information is needed to insure the future protection of public water supply ground water sources.

D. PROBLEMS TO SOLVE

In the past, all the pesticides for which an examination was made during the water supply studies were used on crops. However, over the past five years they have gradually been replaced with new ones. There are too many to enumerate here; however, as an example, a partial list of pesticides recommended in 1970 for potato crop control for the State of New York are listed below.

Seed Treatment	Weed Control	Insect Control	Blight Control
Captan	Per Merge	parathion	Dithane
Polyram	linuron	endosulfan (Thiodan)	Manzate
Dithane	Patoran	carbaryl (Sevin)	polyram
	Eptam		Daconil
	amitrole		Difolatan

Many herbicides in addition to 2,4,5-T, 2,4-D and 2,4,5-TP are used for weed control along highways, railroads, power transmission lines, etc. Following is a list of such compounds that have been used in watersheds that serve as water supplies: Aquathol Plus (disodium 3,6-endoxohexahydrophthalate), Radapon and Dalpon (2,2-dichloro propionic acid), Tordon (4-amino-3,4,5-trichloro picolinic acid), Simazine 80W (2-chloro-4,6-bis-(ethylamino)-s-triazine), Bromacil (50-bromo-3-*sec*-butyl-6-methyluracil).

Expanding the foregoing lists to a nationwide basis, the necessity for constant research relative to the possibility of such chemicals getting into water supplies, surface and ground, is obvious. Such questions as does the chemical persist while being carried through the soil to the wells or over the gound to the reservoir, how far away from drinking water source should the chemical be applied, and most important is the chemical a health hazard when consumed by man through water must be answered.

Another important consideration that metropolitan health officials must consider is the use of irrigation wells as water supply sources as farms disappear and suburbia takes over.

The only drinking water standard that exists to protect the consumer from harmful organic chemicals other than phenols, detergents and those pesticides listed in Table I is the carbon-chloroform extract. Two hundred micrograms of these ill-defined substances per liter of drinking water are allowed. It has been estimated that activated carbon may remove only 10% of the organic matter from water, and chloroform extraction of the carbon does not remove all that is adsorbed. Thus the level of exposure of the public to organics via drinking water is not accurately known. Therefore, probably the greatest problem facing chemists in the field of water hygiene today is the identification of organic compounds, including pesticides, found in drinking water so that proper standards can be set.

FATE OF PESTICIDES IN SOILS AND CROPS

B. J. Stojanovic, Fay Hutto, and W. W. Walker

By definition pesticides are substances or mixtures of substances that may be used to destroy or otherwise control any unwanted form of plant or animal life. The ending -CIDE of the term pesticide means killer. In this regard pesticidal materials are purposely applied to the soil and/or crops to control a wide spectrum of pests such as insects, rodents, plant pathogens, weeds, and others.

Interestingly, control of pests is not a 20th century invention but rather it has been practiced in some rudimentary form from the very beginning of man's existence on the earth or at least as far back as man began recording his history. For example, in the year 1000 B.C. the author of the Iliad and Odyssey, the Greek poet Homer, wrote of sulfur as having "divine and purifying fumigation" properties which can ward off pests.[1] The use of arsenic, which had been assigned similar properties, was suggested by the Roman author Pliny.[1] These chemicals are still in use today either as such or as components of various pesticidal chemicals.

Currently pesticides are used so extensively that the prosperity of Homo sapiens is attributed largely to their effects upon his competitors, the pests. However, contrary to the general agreement that pesticides are necessary for protection of our health and comfort and of our food and fiber supplies, the widespread use of synthetic organic compounds has introduced an unprecedented array of chemicals into the environment. At the same time it has become increasingly more evident that some pesticides have serious short comings, the most widely acclaimed of which are toxicity to non-target organisms and long persistence in the environment. The ability of certain pesticides to appear far from the site of their application and the property to persist and accumulate in soils, crops, and animal tissues (i.e. the movement of pesticide residues into the food chains) give cause for alarm whenever it becomes known that their rate of accumulation in the biota surpasses their rate of breakdown and detoxification. In fact, persistence and toxicity towards non-target organisms determine whether or not a pesticide is desirable, and in due time may be the main basis for a decision about its further usage or discontinuance.

As pesticides in recent years have become man's most relied-upon weapon in his arsenal of weapons in the struggle to control or eradicate pests, the necessary technologies have been developed to serve the needs of agriculture and public health. Obtaining information on the fate of these chemicals in soils and crops, however, has not kept pace with these developments. Clearly, in the past the criteria for selection of effective pesticides has been based on toxicological, economic, and selectivity factors. The reasons were: (1) most agricultural products brought very narrow margins of profit; (2) manufacture and usage of pesticides had to guarantee suitable returns for the investments made; and (3) the pesticide had to control or destroy the target pests. Present emphasis on a pollutant-free environment necessitates critical studies and as thorough an understanding as possible of the fate of various pesticides that tend to be stored in soils and crops. Moreover, as agriculture becomes increasingly dependent on chemistry, the importance of the fate of chemicals in soils and crops will be magnified still more.

This brief review attempts to present a generalized or oversimplified version of certain processes directly or indirectly affecting the fate of pesticides in soils and crops. The effect of soil microorganisms on the fate of pesticides will be emphasized. The reader is advised to consult several excellent reviews on specific topics related to the subject of this review, some of which are referred to in this review.

EFFECT OF PHYSICOCHEMICAL PROCESSES ON THE FATE OF PESTICIDES

Soils represent complex natural systems within which numerous physicochemical and biological processes operate. They are dynamic bodies, consisting of mineral and organic matter, water, and air combined in three phases: solid, liquid, and gaseous. Many different kinds of soils exist throughout the world. Differences from location to location generally reflect changes in topography, drainage, parent material, or some other factor. When soils contain the proper amounts of air and water, they supply mechanical support and, in part, nutrients for crops.

The fate of pesticides applied to crops and soils has been studied for about 25 years. The amount of work has increased exponentially during that time with a very large increase during the past four or five years.

Pesticidal chemicals that are added to the soil may be inactivated, destroyed, or removed from the soil by several processes. The end result of these processes is the detoxification or cleansing of the ecosystem. Such cleansing of the environment involves both physicochemical and biological mechanisms. The physicochemical detoxification may result from: (1) adsorption; (2) movement; (3) photodecomposition, and (4) chemical reaction.

Adsorption of pesticides on soil particles is one of the more important of the deactivating mechanisms because it influences all others.[2] Adsorption is attributed to physical forces (van der Waals), hydrogen bonding, coordination complexes, and chemical forces (coulombic).[3] The extent of adsorption is related to the chemical nature of the pesticide, soil moisture, pH, temperature, type of formulation and individual colloid. In general prediction of pesticide adsorption, especially by the silicate surfaces, is largely empirical. The adsorption of most pesticides could be best estimated from the soil organic matter content, with pH and clay content sometimes being relevant.[3] As a rule of thumb adsorption decreases with increasing pH and temperature, and it is higher in organic than in mineral soils and in heavy textured than in light textured soils. Exceptions, however, are not uncommon. An extensive adsorption does not necessarily mean a tight holding of pesticides to the surfaces of the colloids. Thus, there may be an insignificant loss of activity despite the removal of a substantial amount of the toxic chemical from the soil solution.

Movement is understood as the physical transport of pesticides within and through the soil. The processes are volatilization, leaching, and runoff. Volatilization frequently is the chief avenue by which certain fumigants and a variety of insecticides and herbicides are removed from the soil. Volatilization is dependent on the vapor pressure of pesticides and soil texture, moisture, adsorptivity, temperature, and pH. Based on the existing information it could be generalized that volatilization of pesticides increases with increased temperature and lower clay or organic matter content, and is greater from moist than from dry soils, but becomes negligible as pores become water-saturated.[3] Leaching or the movement of solutes in the liquid phase consists of molecular diffusion and mass transfer. The rate and magnitude of leaching is associated with the amount of water passing through a layer of soil, be it from rainfall or from irrigation. The leaching, or movement by gravity, is dependent upon the physical and chemical characteristics of the soil, the nature of the formu-

lation of the chemical, and the amount of water migrating through the profile. Leaching, runoff, and soil erosion can be the forerunners to pollution of ground water, streams, or rivers. Runoff is the lateral movement of pesticides across the soil surface. Factors enhancing runoff are steep topography, low soil permeability, and intense and/or prolonged precipitation. Since most pesticide runoff is short range on cultivated fields, stream contamination by pesticides in the runoff appears to be unlikely unless it is tied up with extensive soil erosion.

Photodecomposition is the breakdown of pesticidal molecules under the influence of light. Conceivably photodecomposition can occur only on the surface of the soil; therefore, only those compounds applied to the surface or those which have moved to the surface during drying will be degraded. Most research deals with reactions occurring in solution, often organic rather than aqueous. At present photolysis is not well understood, and future endeavors should be centered on establishment of the quantitative significance of photodegradation at the soil surface.

Chemical reactions of pesticides in soil display similarities to those in the test tube. They involve the attack of a reagent on a reactive compound. Because of its structure soil presents an effective medium for the conduct of such reactions because it permits the confluence of oxygen, water surfaces, and pesticides with the soil constituents.[4] Chemical reactions of pesticides may take place independently of soil or they may be soil-catalyzed. Most of these reactions can be classified as either catalytic or hydrolytic. The consensus of opinion among scientists appears to be that the degradation of pesticides in soils by chemical reaction may be a more common process than was previously realized.

EFFECT OF BIOLOGICAL PROCESSES ON THE FATE OF PESTICIDES

The biological processes involved in the detoxification of pesticides in soils and crops involve the activities of soil microorganisms and the uptake and metabolism of pesticides by plants.

Microbial metabolism represents a main channel of degradation and detoxification for many pesticides. Microorganisms are often the sole means of freeing treated soil of foreign chemicals. To the micropopulation many of the pesticides merely represent exotic carbonaceous substrates which are available to a small or large segment of the community as sources of carbon or other nutrients. The availability of a pesticide as a nutrient will determine its slow or rapid dissipation in the soil, the rate depending upon the compound, the method of application, the extent and degree of adsorption, the vigor of the active species, various environmental factors, and possible toxicity of the substrate to microorganisms using it.

Generally the factors that render a pesticide molecule biodegradable are not well understood. Slightly soluble, highly chlorinated pesticides are generally most resistant to microbial attack.[3] Many of the chlorinated hydrocarbon pesticides fall in this category. Pesticides containing polar groups such as OH, NH_2, =N-C(O)-, COO-, NO_2, and a few others often provide a locus of attack to microorganisms. The rate of reaction is further influenced by steric and electronic factors on neighboring atoms.

Whereas the climatic and edaphic factors favoring metabolism of pesticides are well understood, the information on mechanisms by which microorganisms degrade pesticides is quite scant. Presence of organic matter, nearly neutral pH, adequate moisture, and warm soil temperatures generally promote microbial activity and in turn enhance metabolism (biodegradation) of pesticides. Reduction of nitro-groups and displacement of Cl by H represent alternate reactions which may be encountered under water-logged soil conditions. These reactions are also usually more rapid than the oxidative pathways occurring in aerobic environments.

Various substituents and linkages of the chemicals determine the degree of their biodegradability. In this regard some generalizations can be made regarding the effect of "hard" and "soft" linkages. Several linkages which are reported to be readily biodegradable are as follows: carbamates ($R-NH-CO_2R'$), anilides ($R-NH-COR'$), phosphates ($-OOP=O-S-R$, $-OOP=O-O-R$), and aliphatic acids ($R-CHCL-COO-$, $R-CCL_2-COO-$).[5] The rate at which linkages are hydrolyzed will depend on the nature of R and R'. Few investigations have ever attempted to compare the structural features necessary for toxicity to target pests with those permitting degradation in the environment. Some information exists, however, for some of the major classes of pesticides. For example, the most herbicidally active structures of aliphatic acids are also the most readily biodegradable structures. Increasing or reducing the chain length reduces herbicidal activity. Phosphate insecticides display a wide range of stability towards biodegradation but are generally regarded as not persistent. Phenylcarbamate herbicides, on the other hand, are readily broken down by soil microorganisms.

Uptake of pesticides by plants is another biological mechanism which to a degree influences the fate of pesticides in the soil. Both cultivated and non-cultivated plants may assimilate through their roots a variety of pesticides and thereby lower the concentration of these chemicals in the ecosystem. Uptake of pesticides by plants is desirable when the plants are weeds or the pesticides are systemic insecticides or fungicides; it is undesirable when persistent residues remain in portions of the plant used for food or feed. It can be generalized that any organic pesticide introduced into a plant may undergo degradation, modification of structure, or condensation with natural plant constituents. Often a detoxification mechanism may consist of simple conjugation of pesticides with carbohydrates, proteins, amino acids, etc. There are, however, many unknown factors regarding the fate of pesticides in crops. In general the translocation of toxic chemicals throughout the plant depends upon complex and interrelated morphological, physiological, biochemical, and physical factors. The complete picture is quite unclear, as some pesticides are applied in one form, translocated in a changed form, and are inhibitory in still another form. Many other chemicals, however, remain unchanged.

RECENT ADVANCES IN DEVELOPING MORE RAPIDLY DEGRADABLE PESTICIDES

The injurious effects of pesticide use could be most efficiently overcome by completely halting the use of pesticide chemicals and replacing them with biological methods of control. This alternative possibly represents the ideal situation from an ecological standpoint, but many experts believe that it will be years or even decades before biological methods can assume any significant part of the burden of controlling pests. In the interim, they maintain, chemical control is the only answer.[6]

Nonetheless, the dangers involved in the use of pesticide chemicals could be substantially reduced by 1) the selection of alternate, less hazardous pesticides, or 2) the development of new, safer, more selective chemicals.

According to the U. S. Department of Agriculture, more than three-quarters of the organochlorine pesticides used by farmers on cotton, corn, peanuts, and tobacco could have been replaced by less persistent insecticides without affecting production as far back as 1966.[6] However, these alternative pesticides are likely to be more expensive when only the cost of the pesticide material is considered because they may be somewhat less effective against given pests and, therefore, required in larger quantities than the harsh organochlorines.[7] This may in part explain the fact that the use of chlorinated hydrocarbon insecticides has not been curtailed but rather increased since 1966 until federal legislation regulated their use. However, realistic consideration of the cost of any pesticide cannot be based solely on the output required to purchase and apply the pesticide but

must also consider any injurious effects, whether accidental or otherwise.[7] With the organochlorines, for example, costs involved in monitoring for environmental residues must be considered. With highly toxic compounds, costs of medical expenses and time lost through employee illness are factors to be dealt with in determining the overall cost.

A realistic cost/benefit assessment using this approach tends to favor the use of non-persistent pesticides which entail fewer environmental dangers. Further, some experts contend that it is feasible, on the basis of present knowledge, to substitute pesticides of low persistence and toxicity for the more hazardous ones.[7]

The dairy industry, for example, has successfully eliminated the use of persistent organochlorine insecticides in the production of feeds and forages and in the control of insects affecting dairy cattle. Similarly, the USDA has discontinued the use of dieldrin in preference to low-volume malathion sprays for control of grasshoppers, and the use of methoxychlor and sanitation instead of DDT for the control of Dutch Elm disease has drastically reduced the hazard to bird populations.

The use of alternative pesticides, however, may not improve the situation but may, in fact, worsen it.[8] For example, use of Azodrin, a relatively non-persistent organophosphorus insecticide, as a substitute for DDT and toxaphene, both of which are persistent organochlorines, to control the cotton bollworm in the southwestern U.S. resulted in the death of a large number of dove and related birds. Similarly, carbaryl, a relatively non-persistent carbamate insecticide which displays low toxicity to vertebrates, is quite toxic to bees. The use of this compound has resulted in the destruction of many apiaries and consequent damage to pollination of crops and other plants.

In addition, it may be that in some situations the costs involved in the use of alternative pesticides are prohibitive or that suitable substitutes are not available. Under these conditions, one must rely on the development of new, safer pesticides. The cost of developing these new pesticides - an expense which must be realized upon marketing of the product - is staggering. The cost of bringing a single new compound to market has risen from $1,196,000 in 1956 to $4,060,436 in 1969[9] to $5,500,000 in 1970.[6] Moreover, the overall chance of success for an experimental product of this type, one in 1,800 in 1956, has dropped considerably. Estimates of a new product's chance of success on the 1969 market range from one in 5,040[9] to one in 36,000[10] with the latter authors setting the odds for a new product to attain a sales volume of over $5 million/year as only one in 360,000. These estimates clearly illustrate that the search for new pesticides may well meet with diminishing returns.

Despite the increasing chance of economic failure, new pesticides are being marketed, generally for the express purpose of combating environmental pollution. For example, S. B. Penick and Company has produced an insecticidal material trademarked as SBP-1382.[11] This compound is a synthetic pyrethroid produced by esterification of 5-benzyl-3-furylcarbinol, a raw material produced chemically, and cis-trans chrysanthemic acid. It is designed for use in the control of both flying and crawling insects, effects the same degree of insect toxicity as the pyrethrin insecticides, but is less toxic to mammals than the pyrethrins.

Along this same line, research workers at the University of Illinois under the direction of entomologist Robert L. Metcalf have developed seven new insecticidal chemicals.[12] All are DDT analogs and are as effective as DDT against flies and mosquitoes. Two of the analogs, 1,1,1-trichloro-2-p-methoxyphenyl,2-p-methylthiophenylethane and 1,1,1-trichloro-2-p-ethoxyphenyl,2-p-methoxyphenylethane, are especially promising in that they are more selective than the broad spectrum

DDT while equally as toxic to flies and mosquitoes. In addition, DDT-resistant strains of these insects appear to be susceptible to these analogs, while the new compounds are distinctly less toxic to higher animals. The new analogs are also less persistent than DDT and upon degradation they are converted to water soluble metabolites which are rapidly excreted instead of being stored in fatty tissues (as are DDT's water-insoluble degradation-products).

New herbicide formulation and combination promise greatly increased effectiveness and safety in control of aquatic weeds. A combination of 4 ppm of $CuSO_4$ and 1 ppm of diquat gives more effective and prolonged control of hydrilla than 20 ppm of $CuSO_4$ or 3 ppm diquat alone or any of the numerous other herbicides and mixtures that have been tested. The combination assures greater safety for fish, reduces the chemical cost substantially, and greatly diminishes the danger of accumulation of residues in water.[13]

Furthermore, a new granular formulation of an amine salt of endothall provides control of hydrilla comparable to much greater rates of liquid formulation previously used. It confines the chemical residues mostly to the bottom two feet of a lake or pond, reduces the amount of herbicide required, and eliminates or greatly reduces the fish toxicity involved in use of liquid formulations.[13]

Pilot control studies employing short-lasting insecticides were conducted on 14,231 acres in Idaho and Washington. A new stabilized formulation of pyrethrum showed promise in controlling the hemlock looper. Zectran applied in very fine droplets failed to meet control criteria in controlling the spruce bud worm.[13]

Benomyl may be a promising fungicide for the control of Dutch elm disease. Benomyl was readily taken up by the seedling roots and by a newly developed technique, detected throughout the plant. The recent synthesis and development of several synthetic fungicides have given new impetus to the search for chemotherapeutic agents which will control the Dutch elm disease. This approach is especially significant since DDT up until recently has been the major chemical control for this pest.

Recently several advances have been made in the discovery of effective systemic fungicides. One of the materials which is effective chiefly against basidiomycetes (rusts, smuts, bunt of cereals, etc.) is the 1,4-oxathiins.[14,15] Specifically, carboxin (2,3-dihydro-5-carboxanilido-6-methyl-1,4-oxathiin) has shown great promise as a seed treatment for the loose smuts. A closely related derivative, carboxin dioxide (2,3-dihydro-5-carboxyanilido-6-methyl-1,4-oxathiin-4,4-dioxide), is effective against the rusts.[16]

Two benzimidazole derivatives, the TBZ 2-(4-thiazolyl) benzimidazole, and benomyl (methyl 1-(butylcarbamoyl)-2-benzimidazole-carbamate) have systemic properties and are effective against fungi, both foliar and soil pathogens.[17,18]

Even as investigators search for "soft" pesticides to replace the more dangerous compounds, and as suppliers strive to produce new and safer chemicals, there exists a growing trend toward the rejection of all synthetic agricultural chemicals in favor of naturally produced materials, and it may well be that more attention should be focused on natural products for aid in pest control. One facet of this overall area is the use of microbiological products as pesticide chemicals.

In the course of the life cycle of any microbiological population, thousands of chemicals are synthesized, quite a few of which have been found useful in the service of man. The best known of the compounds, of course, are the antibiotics, which inhibit the growth and replication of other microorganisms.[19] Since the mode of action of many antibiotics involves interference with processes basic to all forms of life, it is entirely reasonable that some of these microbial

products should affect the development and functioning of insects. The effect of microbial antibiotics on various insect pests has been thoroughly reviewed.[19]

The codling moth (Carpocapsa pomonella) was found to be quite susceptible to novobiocin.[20] When a 150 ppm solution of this antibiotic was applied topically to female moths, 100 per cent mortality was achieved in three days. Similar results were obtained upon treatment of the green peach aphid (Myzus persicae) with novobiocin. However, novobiocin displayed a selective type of toxicity in that the closely related apple aphid (Aphis phomi) and pea aphid (Acyrthrosiphum pisum) were unaffected. Similar selectivity with respect to target organisms was observed with cycloheximide, which was highly toxic to the rice stem borer (Chilo simplex) and the green peach aphid, moderately toxic to the apple aphid, and non-toxic to the pea aphid.

Xanthomycin and actinomycin A had respective LD_{50} values of 24 and 58 micrograms/insect when administered by ingestion to German cockroaches.[21] The LD_{50} value for xanthomycin, however, was 3.6 micrograms/insect when the antibiotic was injected into the cockroaches, indicating that methods of application are very important factors in determining the insecticidal properties of these compounds. Actinomycin A was not toxic to the black carpet beetle (Attagenus piceus), but did act as a repellent when impregnated in wool fabric.[22]

Considerable effort has been directed toward stored grain weevils and their possible control by antibiotics. Moderate mortality of the granary weevil (Sitophilus granarius) and a rice weevil (Sitophilus oryzae) occurred when the grain was treated with oxytetracycline[23] while streptomycin had no appreciable effect. Chlorotetracycline was highly toxic to two other rice weevils (Calandra oryzae and Calandra sasakii) whereas oxytetracycline was far less effective.

These examples represent but a few of the bacterial antibiotics which, because of their toxicity and selectivity, and because they are produced naturally by biological systems, may well deserve attention as potential insecticidal chemicals. Investigation of the mode of action of these antibiotics in insects has led to the conclusion that, in general, these compounds are toxic because of the disruption of the protein synthesis process, either in production of messenger RNA from DNA or in the actual synthesis of the protein at the ribosomes.[19] Inhibition at either stage, however, would result in no protein synthesis.

One aspect of the overall idea of microbial toxins as insecticides which deserves special attention is the bacterial toxin produced by Bacillus thuringiensis, the first microbial insecticide to be commercially developed. The pathogenicity of this bacterium was originally thought to be due to the presence of either bacterial cells or spores, but it is now clear that the pathological effect of B. thuringiensis is due to the presence of toxins. Germination of spores and multiplication of the organism in the host is a secondary phenomenon.[19] Five toxins are produced by this bacterium. These are (1) parasporal crystals, (2) a thermostable toxin (β-exotoxin), (3) α-exotoxin (lecithinase), (4) proteinase, and (5) a boullogenic antibiotic. However, only the β-exotoxin has a molecular structure simple enough to be characterized fully and produced chemically.

In addition to bacterial species which may adversely affect the life cycle of a given insect, fungi are also active in this regard. Members of the phycomycetes, ascomycetes, and especially deuteromycetes (fungi imperfecti) classes have been known to be pathogenic to insects for many years. Although these pathogens generally destroy their target insect by multiplying rapidly within the insect's body, it may well be that the production of toxic materials is an important part of the infection process, and these chemicals may have the potential for use as insecticides.[19] Little investigation, however, has been done concerning the insecticidal capacities of mycological toxins in the absence of the fungus which produced them.

SUMMARY

In order to feed and clothe all people, man must use pesticides. However, he must also be conscious of the behavior of these harmful chemicals in the ecosystem, especially where their presence might affect his own welfare. Investigations concerning the fate of pesticides in soil have shown that pesticide detoxification proceeds by two mechanisms: physicochemical (adsorption, movement, photochemical decomposition, and chemical reaction), and/or biological (microbial breakdown and plant uptake). However, since many of these studies have been limited in scope and qualitative in nature, considerable research must still be performed to fully understand the ultimate fate of pesticides in soil.

Future development of new pesticides should be concerned with chemicals which are more selective and biodegradable than many of the presently used pesticides. As these new compounds are developed, their behavior in the environment must be determined before they are made commercially available.

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THE NATIONAL PESTICIDE MONITORING PROGRAM

Herman R. Feltz

The National Pesticide Monitoring Program (NPMP) is sponsored by a Monitoring Panel consisting of members appointed from agencies or components in the Departments of Agriculture; Defense; Commerce; Interior; Health, Education, and Welfare, the National Science Foundation; the Environmental Protection Agency; and the Tennessee Valley Authority. Its principal functions are to promote a national pesticide monitoring program, to encourage development and use of uniform sampling and analytical methodology, and to assure that the results of monitoring are effectively disseminated.

Organizational Responsibility

The Monitoring Panel is one of five active panels of the Federal Working Group on Pest Management (FWGPM), whose origin may be traced to the creation of the Federal Pest Control Review Board. The Board was established in 1961 because of the concern of President John F. Kennedy for interagency cooperation in the use of pesticides. This was an advisory board composed of two members from Agriculture; Defense; Health, Education, and Welfare; and Interior. It was charged to provide a joint review of all major federal pest control programs, coordinating the activities of the four departments. In 1964, in response to the 1963 Report of the President's Science Advisory Committee on Use of Pesticides, a charter was signed by the Secretaries of the four departments, creating a new Federal Committee on Pest Control (FCPC). Subcommittees on Program Review, Monitoring, Safety, Research and Information were subsequently added to assist the parent FCPC in its broadened scope and responsibilities.

The replacement of the FCPC by the Working Group of the Subcommittee on Pesticides, President's Cabinet Committee on the Environment was announced by the White House in November 1969. The charter of the Working Group was published in the Federal Register on March 26, 1970. When Executive Plan III became effective in July 1970, the Cabinet Committee on the Environment was dissolved, although the Working Group continued to perform its functions. In October, by White House memo to the Chairman of the Council on Environmental Quality (CEQ), the Working Group on Pesticides was made responsible to CEQ. On November 23, 1971, the Chairman of the CEQ approved a new charter for the Working Group reflecting organizational changes within the federal government, and changing the name of the Group to the Federal Working Group on Pest Management. The following agencies have membership on the Working Group: the Departments of Agriculture; Health, Education, and Welfare; Interior; Defense; Transportation; State; Commerce; and the Environmental Protection Agency. The Council on Environmental Quality, the Office of Science and Technology, the Office of Management and Budget and the Office of Intergovernmental Relations may designate an observer at the meetings of the Federal Working Group. Other agencies may be invited to participate.

The Federal Working Group is the primary staff level coordinating mechanism for federal activities concerning pesticides, pests and pest management. The activities coordinated by the Federal Working Group include but are not limited to:

a. Pest control programs in various parts of the world in which there is active participation on the part of the federal government, either in funding or in supervision;

b. Research on pests and their control and effects of management procedures, whether by chemical or other methods;

c. Monitoring of the environment for pesticides and their residues;

d. Establishment of survey investigation teams to conduct special investigations of problems which arise or which may be anticipated;

e. Public information on pest management and the use of pesticides;

f. Evaluation of economic and social values and risks involved in the control or noncontrol of pests by various methods;

g. Development and coordination of safety measures in the use and disposal of pesticides; and

h. Training programs that will result in an adequate level of competence by federal employees in utilizing and prescribing various control techniques.

The Federal Working Group advises the Council on Environmental Quality and the appropriate federal departments and agencies concerning matters of common interest. In no case, however, does the Federal Working Group supersede the responsibility of each agency to carry out the functions assigned to it by legislative and executive mandates. The Federal Working Group encourages an exchange of information among international, federal, state and local agencies, and participates with them as appropriate.

In due course, the charter of the Monitoring Panel will be rewritten to reflect responsibilities consistent with the charter of the Working Group. Of significance, is that the role of "Monitoring" is succinctly stated, and placed in perspective with charges to the other panels: Program Review, Research, Safety, and Information.

Program Description

The National Pesticide Monitoring Program (NPMP) was first described in the Pesticides Monitoring Journal (PMJ), Vol. 1, No. 1 (1967). The Program was initially designed on the basis of the minimum monitoring needed to establish baseline levels of pesticides in food and feed, humans, soil, water, air, wildlife, fish and estuaries, and to assess changes in these levels. Monitoring activities are subject to continuous change--to incorporate research investigations, utilization of improved methodology, modification to reflect changes in program emphasis, and to accommodate findings within existing programs. In 1968, a review of the components of the National Pesticide Monitoring Program was initiated by the original Subcommittee on Monitoring. Program design criteria were straightforward, calling for component monitoring on a random basis to continually assess pesticide levels and define problem areas. The review has been completed by the Subcommittee's successor, the Monitoring Panel of the Federal Working Group on Pest Management, responsible to the Council on Environmental Quality.

Recent realignments have been made in the pesticide activities of the federal agencies; and, although the focal point of federal policies and activities for environmental monitoring is within the Environmental Protection Agency, many of the monitoring activities on pesticides remain in other agencies. The revised programs were published in the Pesticides Monitoring Journal, Vol. 5, No. 1, June 1971.

The Monitoring Panel defines monitoring as "repeated sampling of environmental components to obtain data on pesticide residue levels in reference to an arbitrarily defined base line." Monitoring of each component in the program is conducted by a federal agency or its cooperators. The design for sampling is reviewed by this Panel of the Working Group to ensure national coverage in terms of defining levels and "problem-finding." Agencies conduct this monitoring as a part of, or in addition to, their own mission-oriented monitoring. Participation in the NPMP, under ever increasing budgetary constraints, exemplifies interagency cooperation.

Details of the monitoring program for each of the components can be examined in the Journal; a summary, however, seems appropriate.

Food and Feed

The Federal program for monitoring pesticide residues in food and feed is comprised of surveillance programs maintained by the Food and Drug Administration. U.S. Department of Health, Education, and Welfare and by the Consumer Protection Program, Consumer and Marketing Service, U.S. Department of Agriculture. The Department of Agriculture is responsible for the sampling of meat and poultry, and DHEW is responsible for raw agricultural products and the Market Basket Studies.

The objective of this program is to determine the levels of pesticide residues in unprocessed and commercially processed consumer food commodities, animal feeds, and composites of food items prepared for human consumption. Programs being carried out to accomplish this objective include (1) a continuing Market Basket Study to determine pesticide residues in the basic 2-week diet of a 16-to-19-year-old male, statistically the Nation's largest eater, (2) nationwide surveillance of unprocessed food and feed, and (3) the surveillance program of the Consumer Protection Program, Consumer and Marketing Service, U.S. Department of Agriculture, for the analysis of meat and poultry samples taken from animals at slaughter.

An emerging and very important objective of this program is to determine levels of contaminants not directly attributable to pesticide application e.g. mercury, polychlorinated biphenyls, cadmium, etc. To the extent that methodology and program mechanics are interrelated with pesticides, determination of such contaminants has become an automatic objective of this program.

Humans

The purpose of the human monitoring program is to determine on a national scale levels of pesticide incidence in the general population and to assess changes in these levels. Such incidence reflects prior exposure from all sources and is important in understanding the ecological impact of pesticides pollution and in studying the human health effects of pesticides exposure. Man may be exposed to pesticides through contact with any of the elements of the environment, including air, water, food, soil, and house dust, as well as in the course of some occupations and hobbies.

Exact measurement of man's total exposure to pesticides requires careful development and implementation of plans, the full cooperation of willing subjects, and adequate laboratory support--conditions which can be attained only in the controlled research situation and are not easily applicable to large groups. Previous human exposure to pesticides may be estimated from measurement of storage levels or excretion of these materials or their metabolites and from measurement of physiologic effects. No one of these approaches can be used to assess exposure to all pesticide chemicals. Some available methodologies are suited to research projects but not to field surveys involving large numbers of samples.

Fish

Beginning in the fall of 1970, 50 new stations were added to the original 50 stations sampled annually by the Bureau of Sport Fisheries and Wildlife for monitoring pesticide residues in fish. The original 50 stations, sampled since the spring of 1967, will be retained in the expanded program.

Three composite samples, each containing 3-5 adult fish of a single species, will be collected. All composite samples will be replicated for a total of 600 samples analyzed annually. Residue analyses will be performed for the identification and quantitation of DDT, DDE, TDE, dieldrin, aldrin, endrin, BHC, heptachlor, heptachlor epoxide, chlordane, toxaphene, mercury, arsenic, and lead. Samples will be screened for the presence of interfering polychlorinated biphenyl compounds (PCB's). Fish will be collected and handled in such a manner as to prevent contamination of the sample with extraneous chemicals.

Wildlife

Early in the development of the wildlife monitoring program, certain criteria were recognized as being important in the selection of species of wild animals suitable for pesticide monitoring purposes. Ideally, the forms selected should be geographically well distributed, and they should be reasonably abundant and readily available for sampling. In addition, animals occurring near the top of food chains have the capacity to reflect residues in organisms occurring at lower levels in the same food chains. Based on these criteria, species chosen for monitoring include the starling (*Sturnus vulgaris*), mallard (*Anas platyrhynchos*) and black ducks (*Anas rubripes*), and the bald eagle (*Haliaeetus leucocephalus*). The black duck is substituted for the mallard in States where suitable numbers of mallards cannot be obtained.

The Bureau of Sport Fisheries and Wildlife is held responsible for the execution of the wildlife portion of the National Pesticide Monitoring Program. The primary objective is to ascertain on a nationwide basis and independent of specific treatments the levels and trends of certain pesticidal chemicals and other pollutants in the bodies of selected forms of wildlife. The program was first described by Johnson *et al.* in 1967. The purpose of this report is to update and redescribe the wildlife monitoring program and briefly review accomplishments.

Estuaries

The estuary is the habitat of a wide array of fish, shellfish, and other biota that have considerable commerical importance as well as value as game species. Terrestrial application of persistent pesticides results in their being carried in surface waters and, through adsorption on silt and debris, transported through river basins eventually into estuaries. Here, their chronic presence at subacute levels might cause irreversible changes before their presence is apparent.

Studies have shown that clams and oysters are particularly well suited for pesticide monitoring; these sessile forms will tolerate chlorinated hydrocarbon pesticides and retain the residues for extended periods following exposure; also, they are abundant and easily handled.

Samples for analyses are collected by agencies at both the Federal and State level from estuarine systems and major river drainages containing commercial quantities of shellfish. In the interest of continuity, uniform sampling procedures are observed by each cooperating organization. A total of 170 stations have been selected for monthly samples of either oysters or clams in 15 coastal States. Sampling points within an estuary are selected on the basis of hydrographic data and the availability of suitable shellfish populations.

Water

The current design of the program for monitoring pesticide residues in the hydrologic environment is a revision of the program initiated in 1967 by the Federal Water Pollution Control Administration and the U.S. Geological Survey and provides for a continuing assessment of the general levels of pesticides in the water and bottom sediments of the Nation's water courses.

Water samples collected quarterly and bed material samples collected semiannually at 161 sites in the conterminous United States, Alaska, Hawaii, and Puerto Rico will be examined for the presence of pesticide residues. Sampling sites were chosen at random from hydrologic units within the major drainage basins defined by the Water Resources Council. Analyses will be performed using separation and identification techniques currently acceptable to the scientific community.

Soils

The agricultural pesticides monitoring program was initiated in 1964 with the establishment of large-scale study areas in the Mississippi Delta; Grand Forks, N. Dak. and Yuma, Ariz. The determination of pesticide residue levels in the soil was an integral part of the study. An additional large-scale study area was established at Mobile, Ala. in the spring of 1965. Also during 1965, the soils phase of the program was expanded to include sampling sites in 17 high-use, 16 low-use, and 18 no-use areas across the United States. The large-scale study areas were phased out at the end of 1967. Selected fields in these areas and the high-, low-, and no-use areas will be resampled periodically.

Results of these pilot studies, including analytical data for soybeans, carrots, peanuts, and potatoes, indicated a need for a nationwide monitoring program to assess the pesticide residue levels in the soils more thoroughly.

The objectives of the soil monitoring program are as follows:

(1) To determine levels of pesticide residues and major pollutants in soils in major land-use areas and other areas in the United States and through periodic sampling, to determine changes in these levels.

(2) To determine the levels of pesticide residues in crops grown on treated soil and other components of the environment directly related to the soil.

(3) To determine the level of pesticide residues in runoff water of certain agricultural lands.

(4) To provide a basis for initiation of special studies on demonstrated problem areas.

(5) To publish the results for appropriate distribution.

Air

Data on pesticides in air should be developed without special consideration for any one sector of the environment such as man, wildlife, etc. In order to do this the country should be divided on an arbitrary basis, i.e. along longitudinal and latitudinal lines or by some other grid mechanism constructed of x number of equally spaced lines east-west and y number of lines north-south across the country. Sampling should be conducted at approximately 60 sites selected by random design.

A rough design for air monitoring can still be devised; however, the limitations of the sampling equipment and analytical procedures selected for use will influence the

length of sampling intervals and the time required for analysis of a sample. These factors will critically affect the number of samples which can be analyzed by a laboratory in a specific period of time.

The Panel notes that the scope of the existing estuarine monitoring program is limited compared to other substrates, which is due in part to the responsible agency's primary mission and resources. Also, there is no operational National Monitoring Program for pesticides in air, and no comprehensive information on this important substrate is developed in other programs. The statement on air monitoring outlines a program needed to develop minimal data which can be correlated with data from other parts of the National Pesticide Monitoring Program.

Summary

Through the NPMP, base-line levels of pesticide incidence have been established in food and feed, humans, soil, water, wildlife, fish and estuaries in order to allow an assessment of changes in these levels. Base lines are needed against which to compare subsequent data to determine what is an increase or decrease in national pesticide levels. Monitoring for a variety of pesticides is conducted in accordance with recognized scientific procedures. A revised list of pesticides suggested for monitoring was published in the PMJ, Vol. 5, No. 1, June 1971, to complement the revised NPMP.

The Program is continually reviewed by the Monitoring Panel to assess necessary changes. Urban soil samples have been added to the soil monitoring component of the program. These, heretofore excluded, were considered to be important in view of the contribution of pesticides from urban sources. Analysis of bottom sediments has been added to the water monitoring program. Most components of the NPMP are now being analyzed for selected environmental contaminants, such as PCB's and heavy metals.

Several articles describing results of the NPMP have appeared in recent issues of the Pesticides Monitoring Journal. As data from other components become available, they too will be published in the PMJ which is a journal of stature among professional workers.

To fulfill the obligation of effective data dissemination, the Monitoring Panel is currently evaluating all available data from each component of the Program for correlation. Such an assessment makes it incumbent upon investigators to provide timely and valid data.

The National Pesticides Program is listed in the Global Network for Environmental Monitoring, developed under the auspices of the National Academy of Sciences, attesting to the merits of program efforts.

DISPOSAL OF WASTE PESTICIDES: PROBLEMS AND SUGGESTED SOLUTIONS

H. C. Johnson and L. P. Wallace

One of the many problems encountered in the disposal of our nation's solid wastes is the handling of toxic and/or hazardous materials including pesticides. Within EPA's Office of Research and Monitoring, the Solid Waste Research Office (SWR) has been and is presently studying effective means of handling and disposing of these hazardous wastes, particularly pesticides. Because of their toxicity, some pesticides must be detoxified before any disposal or reclamation processes can be safely applied, while other pesticides can be disposed of directly. Emphasis in this presentation will be centered on those solid waste management systems which are applicable to, or hold promise for, the disposal of pesticides and pesticide containers.

Land Disposal Methods

The sanitary landfill is currently regarded as the most important land disposal method and consequently, considerable research is directed towards improving this technique and assuring that the environment will be properly protected when this method is used. If correctly located and engineered, one of the most favorable qualities of the sanitary landfill is its ability to receive heterogeneous solid waste loads. These loads vary from being relatively innocuous and chemically inert to being putrescible and even toxic. It is, however, most important that the requirements given in the following definition be met in order for a facility to be considered a "sanitary landfill":

> Sanitary landfilling is a method of disposing of solid waste on land without creating nuisances or hazards to public health or safety, by utilizing the principles of engineering to confine the refuse to the smallest practical area, to reduce it to the smallest practical volume, and to cover it with a layer of earth at the conclusion of each day's operation or at such more frequent intervals as may be necessary.

For every sanitary landfill, and particularly those receiving such toxic materials as pesticide residues, it is important to assure that there is no contamination of nearby ground and surface waters. A Solid Waste Research sponsored study is being performed by researchers at the University of Illinois on the hydrology of several solid waste disposal sites. Data from the study are useful in evaluating the factors that control

ground water and landfill leachate movement. Five different hydrogeologic environments were selected for the study and piezometers were installed in drill holes, strategically located to define fluid potential distribution, and water samples were taken for chemical analysis. In addition to total dissolved solids and chlorides, which are good indicators of leaching, a host of chemical determinations were done on those samples. The results were used to predict the best physical placement of landfills to avoid leaching. No pesticides were detected in the leachate during the time of the study.

At one in-house project, Solid Waste Research is operating a field-scale landfill in Walton, Kentucky, to further study leachate movement and gas formation. The cell being used has been lined with clay and plastic to assure total collection of rainfall or applied water. Information from this study will give further guidance in the safe operation of sanitary landfills for hazardous materials such as pesticides.

Another land disposal system has been under investigation in Alkali Lake, Oregon. Under the sponsorship of Solid Waste Research, scientists at the Environmental Health Sciences Center at Oregon State University have been studying the feasibility of transporting the waste liquor and by-products from 2, 4-D and 2, 4, 5-T manufacturing process to an arid area in Oregon where they are being diluted and applied to the land for natural degradation. The 55-gallon drums used for transporting are chemically cleaned, compressed, and buried or baled and reused as scrap metal. The theory behind the project is that herbicides and pesticides do <u>not</u> have an infinite life in the environment. In every instance where persistence of pesticides in soil has been studied, it has been found that the chemical disappears within acceptable time limits (2-3 years) to a level of little biological significance. The factors causing the disappearance are photochemical decomposition, chemical decomposition, microbiological degradation, and physical factors such as adsorption, volatilization, or leaching. The physical factors, however, only take the pesticides from one place to another, they do not really make them disappear.

Data from trial applications at the site have supported the degradation theory. Application to small plots have shown that very little vertical or lateral movement occurs during the degradation period which has been twenty months for 60 percent degradation. It is planned to start using subsoil injection routinely for the waste liquor presently being stored at the site.

In conjunction with this study, the Oregon State University group is also investigating pesticide container cleanup in Klamath Falls, Oregon. Attempts will be made to chemically clean the containers to such a level that they can be accepted for baling and placement in an electric furnace for scrap metal recovery. Facilities for this study have been constructed and cleanup investigations are presently underway. Liquids from the cleanup operation will either be used as a pesticide or disposed of at the Alkali Lake site. In order to make the container cleanup easier, the researchers have taken an active role in persuading pesticide users

to rinse their containers with water or with the formulation they prepare, adding the rinse back to the prepared formulation. Laboratory tests have shown that rinsing an emptied container three times with several quarts of water reduces the residual pesticide content by 90 percent, affords the user a financial saving of $1/6.5 ounces if the pesticide costs $20/gallon, and greatly facilitates the container cleanup process.

Oceanic disposal of solid wastes, including pesticides and other toxic materials, may be an alternative to the sanitary landfill method; however, there are many questions to be answered before the Solid Waste Research Office could endorse ocean disposal. The report from a contract with the Applied Oceanography Branch of the Dillingham Corporation, San Diego, California, described the nature and magnitude of present ocean disposal practices. In connection with the study, on-site surveys were conducted at 16 United States cities situated on or near the Atlantic and the Pacific coasts, and the Gulf of Mexico.

Data from the study reveal that some 62 million tons of waste are being disposed of at sea each year at a cost of $37 million, including dredging spoils but excluding outdated munitions. Methods employed for disposal consist primarily of transporting the wastes in bulk or barrels aboard self-propelled or towed barges. The majority of wastes are disposed of in bulk form and discharged while the barge is underway. In several cases, highly toxic chemical wastes have been carried to sea aboard merchant ships as deck cargo. The containers were then discharged in undetermined areas once the ship was 300 miles from land. However, bulk industrial wastes are usually transported in tank barges certified for ocean waters by the United States Coast Guard. In addition, United States Coast Guard regulations regarding the bulk shipment of chemicals by water must be adhered to. The Sparkling Waters is just such a barge especially built to handle insecticides and other toxic chemical wastes off the New York coast.

Recently, a final report was received from a contract at Foster D. Snell, Inc. in Florham Park, New Jersey on conditions necessary for decontamination and combustion of organic pesticides and pesticide containers. Work on this project has included:

1. Determining the temperature and rate at which pesticides burn in their pure form while testing the combustion gases for CO, CO_2, H_2O, and intermediate organics.

2. Incorporating the same pesticides in a mass of material such as sawdust, paper, burlap, cloth, polyethylene, and wood, and investigating the burning temperature and rate and determining the combustion products.

3. Low cost chemicals including nitrates and chlorates were incorporated in the pesticide and the pesticide-material mixtures above to facilitate decomposition.

The report indicated the structural and compositional requirements necessary for combustible pesticide containers and the possible use of polyethylene liners to aid combustion. It was shown during the course of the project that representative pesticides were virtually volatilized or sublimed when incinerated unless a binder was present to increase the residence time in the flame. By using polyethylene, which under heating or combustion conditions softens or degrades to products of lower molecular weights, the advantages of a liner and a binder were obtained with one material and the pesticides studied could be essentially destroyed at temperatures normally achieved by burning wood, paper, cardboard, etc.

In all the thermal studies performed, less than five milligram amounts of the pure pesticide chemical were used. Since some undesirable emissions were detected under these conditions, bench and field studies with larger samples need to be investigated before definite conclusions can be drawn.

Destructive distillation (pyrolysis) of pesticides shows great promise as a detoxification reduction method. It should leave an easily handled residue and should thermally degrade effluent gases to acceptable limits. Additional research is needed to verify the possibilities of this method.

A great deal of concern is being directed to recycling of waste material. Some of the present barriers to increased reclamation and recycling are technological in nature and others are economic. Success in overcoming these barriers has the dual advantage of reducing the amount of waste to be disposed of while conserving the nation's natural resources. Cellulosic wastes, including wood, bark, sawdust, oat hulls, corn cobs, bagasse, and other agricultural residues are generated in truly prodigious quantities. Little, if any, significant portion of these wastes is beneficially used and, since they are commonly burned, cellulosic wastes often contribute to air pollution in areas where they accumulate. Under a research grant, the Institute of Forest Products, University of Washington, in Seattle, is developing a unique means for utilizing cellulosic wastes which will at the same time allow safer and more efficient application of pesticides to the soil.

Some common properties of the wood and agricultural wastes are that they consist predominantly of polymeric cellulose macromolecules; they contain an abundance of replaceable hydrogen atoms, and all are biodegradable. Since these waste materials are polymers containing replaceable hydrogen atoms it should be possible to attach pesticides to these substrates in the same way that acetic acid, for example, becomes attached to cellulose in the manufacture of cellulose acetate. Research has shown that pesticides can be attached to such solid waste as sawdust, bark, and lignin by means of ester linkages. Herbicides have been combined with natural as well as synthetic polymers. The herbicides used were 2, 4-D, 2, 4, 5-T, 4(2, 4, 5)-TB, and Dalapon. It was found that each of these polymeric combinations prevented the germination of certain seeds longer than the herbicide alone under controlled laboratory

conditions. Similar results have been obtained in field plots using herbicides and in Costa Rica using the insecticide carbofuran. In the Costa Rican study, it was found that a treatment with the pesticide-polymer combination was effective for eight weeks as opposed to one week for the pesticide alone. Plans are to repeat this study in Puerto Rico where environmental conditions are quite different.

The practical implication of the ability to chemically bond pesticides to cellulosic materials is that very large quantities of cellulosic wastes, so treated, could be utilized as a mulch for gardens and in agriculture. The pesticide in the mulch would be released in controlled fashion with distinct advantages over present procedures for applying pesticides to soils. Now, pesticides usually have rather short useful lives because they may be degraded by bacteria to inactive metabolites, or washed by rainwater into the subsoil where they are inaccessible to pests they are intended to control. Also, and more important from the public health standpoint, this leaching into the subsoil often means that some rather stable pesticides, or their degradation products, find their way into potable water supplies.

In contrast, if the pesticide were chemically combined with the polymeric solid waste, its useful life should be prolonged; attack by bacteria should be reduced; and the pesticide should not be leachable into the subsoil and hence will not pollute streams and rivers. As the solid waste-pesticide mulch lies on and in the soil, it will gradually decompose, continually releasing the active pesticide over a long period of time. With this technique the problems and potential errors of measuring and diluting liquid concentrates are eliminated. Spillages of solids are, of course, less likely than liquid leakages and are easier to rectify when they occur. Controlled releases of the pesticides may also allow lower dosages and fewer applications.

Another very important benefit from this project is the prospect it may hold for development and use of extremely short-lived biodegradable pesticides which, in combination with solid waste polymeric substrates, would be sufficiently stable for practical use. For example, many organophosphorous pesticides are liquid and are too dermally toxic to permit their use by anyone other than an expert. Combinations of these materials would perhaps render them safe, while not destroying their biological activity. The currently "unuseable" pesticides are often effective at much lower dosages than the superficially less hazardous products that are not used in relatively massive amounts.

Composting of municipal and agricultural refuse is not widely used as a means for solid waste disposal in the United States. However, there are several compost plants in operation and one may reasonably expect to see the continued composting of solid waste on limited scale in areas where the product is marketable. A research grant to the Western Research Laboratory of the National Canners Association, Berkeley, California, is supporting a study of the fate of insecticides in composted agricultural wastes. A substantial part of the fruits and vegetables received for

preservation by canning or freezing is discarded as solid wastes. That portion of the raw product which is discarded--vegetable skin and rind--generally has the highest level of insecticide residue, and this fact has limited the use of such material as animal feed, and it also raises questions about possible harmful effects of spreading composted cannery wastes on agricultural lands. This concern is especially justified if toxic degradation or transformation products remain in the compost mixture.

The Canners Association study aims to obtain a better understanding of the mechanism by which insecticides are degraded by microbial or chemical action during aerobic composting, and also to obtain information which will make it possible to dispose of waste materials containing concentrated insecticide residues without hazard to public health. Insecticides selected for the study represent examples of the three principal classes: chlorinated hydrocarbons, organophosphates, and carbamates. The selection of specific insecticides was based upon the extent of usage in agricultural products, variety of chemical structure, and availability of reliable analytical methods. These included: dieldrin; parathion; Diazinon; ρ, ρ^{1}DDT; pentachlorophenol, and with further studies planned for Sevin and Zineb.

During the study, breakdown products of several insecticides have been identified and the varying effects of batch-type and thermophilic composting processes have been noted. The summary in a recent progress report contained the following information:

1. Concentration of Diazinon and parathion rapidly declined in both composting processes with the thermophilic process being the more efficient. Breakdown products identified for Diazinon were oxodiazinon and sulphotepp. Those identified for parathion were aminoparathion, p-aminophenol, and p-nitrophenol.

2. Continuous thermophilic composting caused some reduction in DDT whereas the batch process had little effect. No breakdown products have been identified.

3. Dieldrin was more efficiently degraded in the batch process and none of its breakdown products have been identified.

4. Following the active compost period (120 days), the curing or aging phase (180 days) of the process had little or no effect on the insecticides.

The consideration of pesticide disposal is one facet of hazardous waste disposal. In Section 212 of the Resource Recovery Act, Congress commissioned a study on the feasibility of strategically locating national disposal sites to safely process hazardous materials. The first phase of this two-year study has been initiated through a contract to the Booz-Allen Applied Research Company. Their responsibility is to make a survey and list the quantities, location, generation rate, and present disposal practices of our nation's hazardous wastes. Throughout all the phases of this study, pesticides will be given particular attention in hopes that some safe and effective means of their disposal can be developed.

SAFETY IN HANDLING AND STORING PESTICIDES

James J. Boland

In any given year a number of people become ill or die as a result of overexposure to pesticides. The circumstances of exposure may include, among others, the child who finds a pesticide improperly stored or carelessly placed in use and eats or drinks it, or a workman in a formulating plant or farmer in the field who accidentally spills a pesticide on himself but does not take the necessary action to decontaminate himself and seek medical aid. Regardless of circumstance, most of the illnesses and many of the deaths associated with pesticides could have been avoided.

Although our attention this morning will focus on safety precautions for the worker and applicator of pesticides, perhaps a word should be said about the occasional user of pesticides, the homeowner or weekend gardener. Although not desirable nor totally justifiable, the availability to the homeowner of concentrates of pesticide materials, some in the area of eighty percent, is easily documented by a casual perusal of existing pesticide stock in some retail outlets.

In this instance, the product label is the best source of information. The product label is an excellent source of information. Utilization in this case is synonymous with reading the label. The information contained on the label represents an investment on the part of the manufacturer of 4 to 6 million dollars.

The label gives such information as active ingredient(s), mixing and application rates, target organisms, indication of toxicity, warnings and specific treatment in case of poisoning.

Frequently illness follows when the label is not read. State Services Branch workers[1] have shown that sources of product information are frequently friends, merchants, etc., the information being passed by word of mouth. This circumstance will tend to predispose the user not to read the label or the product may be transferred from friend to friend via the "Coke" bottle route, often with tragic consequences.

In considering safety concepts in the manufacture, formulation, storage, transport and application of pesticides, our approach should be to minimize worker hazard and preserve the integrity of the environment. It is under the conditions of manufacture and formulation that the danger of exposure is greatest, for these conditions usually involve the handling of concentrated materials.

How may we insure worker safety under these conditions? Perhaps we want to consider two approaches--one direct, the other indirect. The indirect approach may include, but is not limited to, the following:

(1) Education - We will presuppose that the manufacturer or formulator is knowledgeable concerning safe handling procedures. (This is something which you may have to determine to your own satisfaction.) A worker who understands the dangers of the product(s) with which he works will readily recognize the importance and necessity of the precautions he is to take. He can do much to insure his own safety. Toxicity, routes of absorption, signs and symptoms and instruction to seek medical aid if he has or thinks he has had an exposure, are points to be incorporated into his educational program.

(2) Personal hygiene - By stressing such factors as washing prior to eating/smoking, daily shower and clothes change, much can be done to insure worker safety.

(3) Medical supervision - Periodic testing of blood cholinesterase activity and/or metabolite excretion will generally serve to detect trouble in a worker who is experiencing an undue exposure and is in danger of perhaps developing a toxic illness.

Protective devices and clothing which physically prevent exposure to pesticide materials are classified, for the purpose of this discussion, as direct methods designed to minimize hazards associated with pesticide processes.

Routes of entry--dermal, oral and respiratory--are all important to the worker. The dermal route of exposure is the most significant to persons involved in the manufacture, formulation or application of pesticides. Wolfe[2] and his coworkers in Washington State have shown in a study of several hundred pesticide applicators that over 97 percent of the pesticide to which the body was subjected was deposited on the skin. This was especially true of applicators applying liquid sprays. The importance of protecting the body surface from contamination is obvious.

Factors such as fatigue, carelessness, boredom with the routine of many plant operations and the sheer bulk of many of the pesticide product elements would be important considerations when we consider the causes of some spills. Gross contamination of workers and their environment is the end result, with concomitant health hazards.

Work by Maibach and Feldmann[3] in California showed that pesticides are more readily absorbed from some body areas than others. Using C 14 labelled parathion as a representative compound, these investigators found the range of absorption to be from 9 percent forearm to 100 percent in the scrotal area. Saturation of clothing with parathion or like substances that are readily absorbed across the intact skin through spillage or saturation by sprays would be akin to an injection of the material directly into the vein.

The importance of this last observation takes on added importance when we think for a moment about the tendency to carry objects or packages which are heavy or unwieldy in the so-called "gut" carry position.

While cloth provides some degree of protection, waterproof trousers are recommended. A waterproof apron would be second choice. Daily changes to clean clothing and daily shower are both important adjuncts to direct protection of the lower body.

Absorption is somewhat less efficient over the upper body; this area still has a significant exposure potential because of the large body surface. A waterproof jacket or raincoat with long sleeves and a close-fitting neck should be used. This gives protection to the upper back, shoulders and forearms of the worker.

The principal objection to the types of protective gear we are speaking about is that in hot weather it becomes very uncomfortable. Worker comfort is in fact an important consideration. Worker discomfort will frequently result in our "well protected man" being seen by mid-morning wearing a T-shirt and baseball cap. What should be encouraged under extreme heat conditions is at least insuring minimal protection by use of a long-sleeve, GI-type cotton twill shirt which should be laundered after each use and changed when it becomes wet with spray. This should never be considered adequate protection, but merely a compromise between nothing and at least minimal protection.

Protective clothing of the lighter colors can be as much as 8 - 10°F cooler than the familiar black or dark green type.

In the head and neck area, Maibach et al. found absorption of parathion to be 32 - 47 percent of the applied dose.[3]

Headgear with a bill or brim will give some protection to the scalp, face and neck area. A waterproof hat with a wide brim is available that affords good protection to this area of the body.

Goggles and respirators provide considerable protection to the face area but should be properly cleaned, serviced and stored.

The high potential exposure to the hands emphasizes the need for wearing globes. Cloth-type gloves are not recommended as they can become soaked with pesticides and then enhance--not prevent--exposure. Rubber gauntlet-type gloves provide the best protection. The gauntlet should cover the wrist, and the glove can be turned out for easy cleaning.

Waterproof shoes or boots provide the best protection for the feet. The trouser leg should be worn outside the boot or shoe top to prevent runoff from going into the boot. Leather work boots become dried and crack when repeatedly soaked with pesticide liquids; this makes them unacceptable as protective gear when handling toxic materials such as pesticides.

Adequate respiratory protection for most types of application is provided by the use of cartridge-type respirators. In some instances, such as manufacture or formulation of extremely toxic products, self-contained or supplied-air type breathing apparatus is used. The oral route of exposure probably is not one of major concern in occupational exposure. It is usually difficult to make a clear distinction between oral exposure and respiratory exposure. Few workers would intentionally eat these products with which they work. Pesticide residues may be on the hands and transferred to lunch or snack items. Therefore, washing before eating and smoking is the best prevention for this type of exposure.

Let us now consider the safe handling of pesticides in other important areas--transportation and storage.

Pesticides may be shipped as the technical material--usually this is the undiluted chemical of up to 95% pure material--or as formulations which are mixtures in which the technical material is combined with a carrier or solvent permitting conventional application.

Hazards to workers in the event of a spill in transit, occur through the same mechanisms as those considered earlier. That is, they may be absorbed, inhaled or ingested. This may occur through contamination of items which are co-shipped or during the cleanup process. Ingestion may occur if contaminated foodstuffs are allowed to reach consumers. Pesticides cannot be shipped with foodstuffs unless they are packaged in air-tight wrappings. Unfortunately this regulation is sometimes ignored or wrappings break and the danger of secondary poisoning still exists.

Cleanup involving pesticides should be performed only by authorized persons. These persons should use adequate measures to protect themselves in the situation including measures discussed above.

The National Agricultural Chemicals Association has formed a network of safety teams to minimize the risk of injury from the accidental spillage or leakage of pesticides.

This network became operation in March of 1970. By contacting a central telephone number (513 961-4300), the team network insures that expert help will be dispatached to the scene of an accident. The safety team network furnishes personnel, equipment and expertise, to insure prompt, efficient cleanup and decontamination following major accidents involving pesticides.

Another form of assistance in general chemical emergencies is the establishment and function of the Chemical Transportation Emergency Center (CHEMTREC), established by the Manufacturing Chemists Association (MCA).

The CHEMTREC number is 800 424-9300; in Washington, D.C., the number is 202 483-7616.

The Department of Transportation, Office of Hazardous Materials is assisting in the dissemination of information concerning the newly established central information point for Chemical Transportation Information (CHEMTREC).

The Chemical Transportation Emergency Center (CHEMTREC) provides emergency personnel with information on safety measures in handling hazardous chemicals involved in accidents on the nation's highways, railroads and waterways. A voluntary program of the Association, which has 165 U.S. member companies, CHEMTREC operates on a 24-hour basis, seven days a week with a nationwide telephone number.

CHEMTREC is not a source of general chemical industry information, such as how to locate a missing shipment; nor is it a policing agency. It is a source of assistance to official organizations concerned in chemical transportation emergencies and is designed to provide immediate data on how to handle these emergencies to those who are trained to do so. The Manufacturing Chemists Association initiates this new program to protect emergency crews and the public has been in development for the past 15 months.

Further information may be obtained by writing either the MCA or the Department of Transportation, Washington, D. C.

The danger of fire in warehousing pesticides is a major public health hazard. Fires involving pesticides are especially hazardous because of the possibility of poisoning from vaporized chemicals added to the usual fire hazards of smoke inhalation and thermal burns. Containers of pesticides rupture. Water and chemicals used to fight the fire spread contaminants over a wide area. Heat and air currents combine to vaporize pesticides and cause them to enter the air. Fire fighters must take extraordinary precautions to avoid breathing fumes and smoke from ignited storage areas and avoid body contact with water and debris.

To summarize, the overriding theme put forth in the preceding pages has hopefully been one of common sense practice when dealing with pesticides or other hazardous chemicals. By using either the direct or indirect approaches to safety, or a combination of the two, we can expect to substantially reduce or eliminate the risks incurred when using toxic chemicals such as pesticides.

References

1. Unpublished data furnished by State Services Branch technical assistance projects.

2. Wolfe, H. R. Protection of Workers from Pesticide Exposure. Proceedings of the Training Course "Pesticides and Public Health (Advanced)" January 18-20, 1971, pp.117.

3. Maibach, H. I.; Feldmann, Robert; Milby, Tom; Serat, William. Proceedings of the Symposium sulla prevenzione delle dermatosi professionali tenutosi, a Monte Porzio Catone, Italy, 25-26 March 1970, pp. 61-64.

PROPOSED FEDERAL PESTICIDE LEGISLATION

Emerson R. Baker

Soon after the Environmental Protection Agency was established (December 2, 1970) by Reorganization Plan No. 3 of 1970 the Administration prepared the "Federal Environmental Pesticide Control Act of 1971," which was introduced on February 10, 1971, by Congressman Poage (Texas; Chairman, Committee on Agriculture) as House Bill No. 4152. An identical bill was introduced on the same date in the Senate as S. 745 by Congressman Packwood (Oregon).

The bill provides two changes in existing pesticide legislation:

First, it amends the Federal Insecticide, Fungicide, and Rodenticide Act to incorporate additional authorities relating to pesticide registration, such as factory inspection, registration of establishments, record keeping, stop sale or use orders, indemnities, and classification of all pesticides as being either general use or restricted use.

Second, it enters a completely new area of Federal control over pesticides by requiring all persons who wish to use a restricted pesticide to be certified by either the State or Federal Government as being competent with respect to the use and handling of such chemicals.

Extended hearings were held in the Committees on Agriculture of both Houses of Congress and hearing reports prepared and published.

The House Committee on Agriculture made substantial changes in the original Administration bill and a few additional changes of the Committee's Bill (HR 10729) were made on the floor of the House. The bill, as revised, was passed by the House on November 9, 1971. As of 1/1/72 the bill has not as yet been released from the Senate Committee on Agriculture and Forestry, and further changes could be made.

The bill (H.R. 10729) itself is divided into four parts (sections). Part one is the title (Federal Environmental Pesticide Control Act of 1971). Part two constitutes the major part of the bill and is in the form of a complete amendment to the Federal Insecticide, Fungicide, and Rodenticide Act (of 1947). It, in fact, cancels the present FIFRA and rewrites a new FIFRA containing 27 sections.

Selected excerpts from the Committee report* are of interest:

<u>Section 1. Short title [FIFRA] and table of contents</u>

<u>Section 2. Definitions</u>
Section 2 includes many of the definitions in the present FIFRA, with several important changes.
A "certified pesticide applicator" is one certified by the State or Federal government according to standards prescribed by the Administrator to use restricted use pesticides.
A "private pesticide applicator" is a certified applicator who uses restricted use pesticides only on his property, or on the property of another without compensation.

*Committee on Agriculture: Report together with additional views to accompany H.R. 10729 [Federal Environmental Pesticide Control Act of 1971]. H.R. Report No. 92-511, Sept 25, 1971.

A "commercial pesticide applicator" is any certified applicator other than a private applicator.
The definition of "misbranded" is amended to include requirements based on other provisions of the Act. For example, labels must bear an establishment registration number and use classification.
"Protect health and the environment" is defined, and includes the requirement to take into account the public interest. "Substantial Adverse Effects on the Environment" contains the same requirement.

Section 3. Registration of pesticides
[This section] requires that all pesticides in the channels of U.S. trade must be registered with the Administrator. Under present law only those pesticides in interstate commerce must be so registered...
... provides authority for the classification of pesticides and where applicable the imposition of restrictions on their use.
... a pesticide may be classified for general use, for restricted use, or both. In the case of a pesticide registered for both general and restricted use the bill requires that directions for each be separate and distinguishable.
... a general use pesticide is one which the Administrator has determined will not cause substantial adverse effects on the environment when applied in accordance with its directions for use and warning or caution statements.
... a restricted use pesticide is one which the Administrator has determined could cause substantial adverse effects on the environment without additional regulatory restrictions...
... when the pesticide presents a hazard to the applicator or other persons, it must be used only by or under the supervision of a certified pesticide applicator or be subject to other regulatory restrictions.
The foregoing classification and restriction constitute entry of Federal regulation into a significantly unregulated area. General use pesticides will be regulated as all pesticides under Federal jurisdiction are regulated at present...

Section 4. Use of restricted use pesticides; certified applicators
This section provides for Federal or State certification of pesticide applicators according to standards prescribed by the Administrator. A State may certify applicators if a plan submitted by the Governor is approved which designates a State agency to administer the plan; assures legal authority, adequate funds, and qualified personnel to execute the plan; provides for reports to the Administrator; and contains applicator certification standards at least equal to those prescribed by the Administrator...

Section 5. Experimental Use Permits
The Administrator may issue, under terms and conditions established by him, experimental use permits if an applicant needs such permit in order to accumulate information necessary to register a pesticide. Such permit may be revoked if its terms or conditions are violated or are inadequate to avoid substantial adverse effects on the environment.

Section 6. Administrative review: suspension
Section 6 provides for the cancellation of a registered pesticide at the end of each five year period unless the registrant requests that the registration be continued. If a pesticide is otherwise cancelled for cause or the classification is changed the registrant may make corrections or file objections and request a public hearing. . ..
Language in the bill relating to scientific advice would maintain a role for scientific advisory committees of the National Academy of Sciences equivalent to that in the present provisions of FIFRA...

Section 7. Registration of establishments
Products subject to the Act must be produced in establishments which are registered with the Administrator. The producer who operates an establishment must inform the Administrator within 30 days after it is registered of the types and amounts of pesticides and devices which he is currently producing, produced during the past year, or which he has sold or distributed during the past year....

Section 8. Books and records
The Administrator may prescribe regulations requiring producers to maintain such records with respect to their operations and the products produced as are necessary for enforcement of the Act. Such records required do not extend to financial data, sales data other than shipment data, pricing data, personnel data, or research data (other than data relating to registered pesticides or to a pesticide for which an application for registration has been filed)....

Section 9. Inspection of establishments
For purposes of enforcing the Act officers or employees duly designated by the Administrator are authorized to enter any establishments at reasonable times to inspect and obtain samples of any pesticides or devices, packaged, labeled, and released for shipment, and samples of any containers or labeling for such products...

Section 10. Protection of trade secrets and other information
Section 10 of the Act provides that an applicant for the registration of a pesticide may mark any part of the data submitted which in his opinion are trade secrets or commercial or financial information and submit such material separately from the other material required.
The Administrator would not make public any such information which in his judgment contains or relates to trade secrets or commercial or financial information...

Section 11. Standards applicable to pesticide applicators
This section exempts private pesticide applicators from any record keeping or report filing regulations prescribed by the Administrator under the Act, and provides that the Administrator shall establish separate certification standards for commercial and private applicators.

Section 12. Unlawful acts
This section includes many prohibited acts from present law and is expanded to cover intrastate acts and to prohibit violations of the provisions of the Act. Among the new prohibitions is refusal to permit lawful inspection of an establishment or sampling of a pesticide; advertisement of a restricted use product not containing such classification; making available for use, or using, a restricted use pesticide other than as provided under the Act or inconsistent with its labeling; and violation of a "stop sale, use, or removal" order...

Section 13. Stop sale, use, removal, and seizure
Subsection (a) of this section authorizes the Administrator to issue a "stop sale, use, or removal" order to any person possessing a device if he believes that the pesticide or device is or will be sold in violation of the Act or if the registration has been suspended or is subject to a final cancellation order...

Section 14. Penalties
H.R. 10729 contains provisions for civil penalties. Such provisions are not included in the existing FIFRA. Persons violating any provision of the Act would be subject to a civil penalty of not more than $5,000 for each offense, except that a private pesticide applicator would be subject to only a $1,000 penalty, and only after receiving a written warning or citation for a prior violation. No civil penalty could be assessed until the person charged has been given a notice and an opportunity for a hearing in the county, parish or city of his residence...

The reported bill also provides that any person who knowingly violates any provision of the Act shall be guilty of a misdemeanor and on conviction be fined not more than $25,000 or imprisoned for not more than one year or both, except that a private pesticide applicator could be fined not more than $1,000 or imprisoned more than 30 days, or both.

Section 15. Indemnities

Subsection (a) provides that if the Administrator notified a registrant that he has suspended the registration of a pesticide because such action is necessary to prevent an imminent hazard and such registration is cancelled as a result of a final determination that the use of such pesticide will create an imminent hazard, any person owning any such pesticide before the suspension notice and who suffered losses because of suspension and ensuing cancellation would be entitled to an indemnity payment.

...The amount...would be determined on the basis of the cost of the pesticide...

Section 16. Administrative review; judicial review

Except as otherwise provided by this section, chapter 5 of title 5 of the U.S. Code relating to administrative procedure and chapter 7 of title 5 of the U.S. Code relating to judicial review apply in respect of rules, rule making, orders, adjudication, licensing, sanctions, agency proceedings, and agency actions under the Act...

The district courts of the U.S. are vested with jurisdiction to enforce and to prevent and restrain violations of the Act...

Section 17. Imports and exports

Subsection (a) exempts from the provisions of the Act an exported pesticide or device which is in accordance with the specifications of the foreign purchaser.

Subsection (b) requires the Administrator to transmit through the State Department to foreign governments and international agencies notice of pesticide registration cancellations.

Subsection (c) provides for the inspection of samples of imported pesticides and devices provided by the Secretary of the Treasury to the Administrator, and for the refusal of admission of a pesticide or device upon a finding by the Administrator that it is in violation of the Act...

Subsection (d) requires the Administrator to participate in international efforts to develop improved pesticide research and regulations...

Section 18. Exemption of Federal agencies

This section authorizes the President to exempt a Federal agency from the provisions of the Act if emergency conditions so require...

Section 19. Disposal and transportation

Section 19 provides that the Administrator of the Environmental Protection Agency shall, after consultation with other interested Federal agencies, establish procedures and regulations for the disposal or storage of excess amounts of such pesticides. The Administrator would be also required to accept at convenient locations for safe disposal a pesticide the registration of which has been cancelled under section 6(c) if requested by the owner of the pesticide...

Section 20. Research and monitoring

This section authorizes the Administrator to use necessary means to undertake pesticides research, giving priority to biologically integrated alternatives to chemicals for pest control; to establish and implement a national plan for monitoring pesticides, as well as undertake other monitoring activities necessitated by provisions of the Act.

Section 21. Solicitation of public comments
... The Administrator may solicit views of all interested parties and seek such advice from "scientists," farmers, farm organizations, and other qualified persons as he deems proper.

Section 22. Delegation and cooperation
This section authorizes the delegation of authorities vested in the Administrator under the Act to his designees, and provides for cooperation by the Administrator with other Federal agencies and with agencies of State and local governments in carrying out the Act.

Section 23. State cooperation, aid, and training
This section authorizes the Administrator to enter into cooperative agreements with States for purposes of enforcement of the Act, including training of personnel and including grants for enforcement programs, and to assist States in establishing applicator certification programs. Further, he may enter into contracts with Federal and State agencies for the purpose of encouraging certified applicator training.

Section 24. Authority of States
This section specifies the authorities retained by the States under the Act. Generally, the intent of the provision is to leave to the States the authority to impose stricter regulation on pesticides use than that required under the Act.

Subsection (a) gives States the authority to regulate the sale or use of a pesticide or device so long as such regulation does not permit sale or use prohibited under the Act...
Subsection (b) preempts any State labeling or packaging requirements differing from such requirements under the Act.
Subsection (c) provides the Administrator with authority to certify a State for the purpose of registering pesticides formulated for intrastate distribution to meet specific local needs. The purpose of this subsection is to give States the opportunity to meet expeditiously and with less cost and administrative burden on the registrant the problem of registering for limited local use a pesticide needed to treat sudden pest infestation.

Section 25. Authority of the Administrator
Subsection (a) of this section authorizes the Administrator to prescribe regulations to carry out the Act.

Section 26. Severability
This standard severability section ...provides that... the invalidity of one "section" does not affect the validity of the others.

Section 27. Authorization for Appropriations
This section authorizes appropriation of such sums as may be necessary to carry out the provisions of the Act for fiscal years 1972, 1973, and 1974...

Part three of the bill amends the "...Federal Hazardous Substances Act, the Poison Prevention Packaging Act, and the Federal Food, Drug, and Cosmetic Act to change the term "economic poison" to the term "pesticide" in order to reflect the change in FIFRA."

Part four of the bill establishes a time table for implementing the Act after passage. Of particular interest here are the following provisions:

...one year after...enactment...the Administrator shall have prescribed the standards for the certification of pesticide applicators...

...within three years after...enactment...each State desiring to certify pesticide applicators shall submit a State plan to the Administrator [on approval]...

...a period of four years from date of enactment shall be provided for certification of pesticide applicators...[and any requirement that a pesticide can be used only by a certified applicator shall not take effect until four years from enactment].

PESTICIDE USE PATTERNS AND SAFETY ASPECTS

Dr. L. C. Gibbs

Pesticide use patterns, like our way of life, have changed significantly over the years. Time was when our arsenal of pesticides consisted of soap, sulfur and tobacco dust. Paris Green was added in 1860; lead arsenate in 1890. This was followed by calcium arsenate in 1919 when some 3 million pounds were used for boll weevil control on cotton. These developments alone point up the fact that we have been experiencing changing pesticide use patterns for years. Needless to say, even more significant changes can be expected in the years ahead as we anticipate population increases, shorter work weeks, more leisure, and increased concern over environmental quality. Coupled with future expectations, it is essential that we note and consider other factors which have and will continue to exert a major influence on our pesticide use patterns in the years ahead. Some of the more important of these are: Public Sentiment, Legislation, Regulations, Research, Technology, Agricultural Systems, Pest Resistance, Residue Tolerances, Lawsuits, Availability of New Pesticides, Pesticide Formulations, Safety Requirements, and others.

Today everyone pretty well generally agrees that pest control is essential for protecting man, plants and animals from diseases, discomforts or annoyances, and for insuring the production of an adequate and economical supply of high quality food, feed and fiber. At the same time, many people are demanding that many pesticides be banned. Irrespective of this, you and I know that consumers would not be willing to accept more costly lower quality foods. This poses some real questions which will require study and a reevaluation of our sense of values, attitudes, and a willingness to accept a middle ground position without sacrificing quality.

Documentation of the future need for pesticides is found in reports of - The Ribicoff Committee (1964); National Academy of Science, Food and Feeds (1968) and Persistent Pesticides (1969); the Mrak Commission (1969); and elsewhere. These reports pointed up existing and potential problems, many of which we are having to cope with today. Increasingly, our emphasis in the years ahead will be placed on research, regulation, education and operating programs which practice and encourage the use of the most effective means of pest control and/or management that will cause the least potential hazard to man, animals, plants, fish, wildlife and other components of the environment. This means that many of the chemical uses producers have been accustomed to in past years have already or soon will be lost. Cancellation of certain uses of DDT, 2,4,5-T, Aldrin, Dieldrin, Mercurial fungicides and other persistent pesticides are cases in point.

Today, pest control in the United States is practiced in a setting of a population growing in numbers, density and affluence and with an intensified monocultural system of agriculture that is employing fewer and fewer persons. In the early years, a farmer produced only enough food for his family and about three others; today, he produces enough for his family and about 45 others.

In order to grasp the full significance of some of the developments that have taken place which have been instrumental in effecting changes in our pesticide use patterns, we need only to recall some of the major changes that have taken place in agriculture. Perhaps the first one we should note is that in the early history of agriculture, farming was diversified and our pest control knowledge and chemicals were limited to say the least. Even in the early 40's, we could still count our pest control materials on our fingers and the commonly available materials included items such as lime sulfur, Paris green, lead arsenate, nicotine sulfate, Rotenone and a few others. In contrast today, our pest control arsenal consists of about 250-300 agricultural chemicals available in some 35,000 registered products. Needless to say, almost everything has changed. Foremost among the factors which have been influencing changes in pesticide use patterns has been the shift toward development of an intensive monoculturistic system of agriculture. This system, for the sake of economy, has resulted in the concentration and culture of large blocks or acreages of a single or successions of the same crop. This alone has been conducive to a build-up of certain pests which required more pesticide use and in some cases resulted in the development of resistance to certain pesticides within some insect species. Increased production costs resulting from labor shortages, increased labor costs, etc. have also been conducive to mechanization and this in turn has fostered increased plant populations which further contributes to increased insect and disease problems. So you see, the circle goes round and round and never stops or stands still. Other factors include the passage of more stringent regulations and laws governing the registration, transportation, sale and use of pesticides, lowered residue tolerances, and the development of the carbamate and systemic type pesticides. One other factor which I have so far failed to mention specifically is the advances made in our analytical equipment and technology. Each factor or combination of factors in turn affects use patterns one way or another and the full impact or change can seldom be fully determined because of the complexity and interaction involved.

Any discussion of changing pesticide patterns would be remiss without some mention of use statistics and recent legislative and regulatory developments. First let's look at some aspects of use statistics since this is undoubtedly the area which has contributed most to some of our problems. Use, likewise, has without question been the paramount factor responsible for the tightened legislative and regulatory actions which have been effected in the last few years. In looking at use statistics, I think that it is important that we look at the volume used and note the use trends developed within the three major classes of pesticides and within even a single class. The following tables, which are more or less self-explanatory, show what the use patterns and trends have been over the years for pesticides as a whole and for some within a group or class. See Table 1 for statistics on pesticide sales volume for fungicides, herbicides and insecticides. Table 2 is illustrative of trends and use patterns developed for the organochlorine type insecticides.

Table 1. Sales of organic pesticides by primary chemical manufacturers according to type of usage, 1963-1970.

Type of Usage	1963 Amount	1963 % of Total	1964 Amount	1964 % of Total	1965 Amount	1965 % of Total	1966 Amount	1966 % of Total
	(Volume of sales in 1,000 pounds)							
Fungicides	93,265	14.3	95,556	13.8	106,342	13.9	118,397	14.4
Herbicides	122,872	18.9	152,027	21.9	182,869	23.9	221,502	26.9
Insecticides	435,334	66.8	444,772	64.3	474,694	62.2	482,357	58.7
TOTAL	651,471		692,355		763,905		822,256	

Type of Usage	1967 Amount	1967 % of Total	1968 Amount	1968 % of Total	1969 Amount	1969 % of Total	1970 Amount	1970 % of Total
	(Volume of sales in 1,000 pounds)							
Fungicides	120,413	13.4	129,961	13.5	121,418	13.4	128,859	14.6
Herbicides	287,582	32.1	318,554	33.2	311,157	33.5	308,112	35.0
Insecticides	489,368	54.5	511,116	53.3	493,088	53.1	443,943	50.4
TOTAL	897,363		959,631		925,663		870,314	

Table 2. Organochlorine insecticides: Producers' domestic disappearance of selected kinds by crop year, United States, 1955-1970.

Crop Year 1/	Aldrin-toxaphene 2/ group	DDT	BHC	Total
	Volume in 1,000 pounds			
1955	54,400	61,800	7,800	124,000
1956	61,570	75,000	9,450	146,020
1957	52,500	71,000	6,600	130,100
1958	78,834	66,700	5,500	151,034
1959	73,331	78,682	4,276	156,289
1960	75,766	70,146	5,111	151,023
1961	78,260	64,068	4,577	146,905
1962	82,125	67,245	2,404	151,774
1963	79,275	61,165	1,299	141,739
1964	83,161	50,542	3/	133,703 4/
1965	80,568	52,986	3/	133,554 4/
1966	86,646	46,672	3/	133,318 4/
1967	86,289	40,257	3/	126,546 4/
1968	38,710	32,753	3/	71,463 4/
1969	89,721	30,256	3/	129,977 5/
1970	62,282	25,457	3/	87,739 5/

1/ Ends September 30.

2/ Includes aldrin, chlordane, dieldrin, endrin, heptachlor, Strobane and toxaphene.

3/ Not published separately to avoid disclosure, but probably less than in 1963.

4/ Includes only the aldrin-toxaphene group and DDT.

5/ Calendar year data.

The use of persistent pesticides underwent more intensive discussion in 1969 than ever before. Although pesticides have contributed tremendously to preventing human disease and to increasing the production of food and fiber, mounting evidence indicated the need for concern about unintended effects on the environment, including injury to the health of man and livestock. Associated with the benefits from the use of pesticides are the risks of injury; and these risks are greater from the use of persistent chemicals. Restrictions have now been placed on the latter with special emphasis on DDT. Coupled with this have been numerous State legislative actions which relate to pesticide use, sale, record-keeping, applicator licensing, development of restricted use categories, etc. In this respect it is of interest to note that as of November 1970, 36 States had enacted pesticide applicator licensing laws. Other significant developments include complete restriction on the use of DDT in a number of States and the development of lists of chemicals limited to restrictive or permit uses.

The major persistent pesticides are commonly known as "organochlorine" compounds ("chlorinated hydrocarbons" or "polychlors"). They include aldrin, benzene hexachloride, chlordane, DDD, DDT, dieldrin, endrin, heptachlor, lindane, toxaphene, and certain others. Compounds containing arsenic, copper, lead, and mercury are also persistent.

In recent years, DDT has become a prime target of concern. Its usage began earlier and has been more widespread than that of other major persistent pesticides. For well over two decades, DDT has been the most generally effective and most widely used pesticide worldwide. It is best known for practically wiping out malaria in the United States and over large areas elsewhere. It has been a valuable tool in combating cholera, typhus, Rocky Mountain spotted fever, and encephalitis. Uninhabitable areas have been made more habitable and life has been made more comfortable for many people. DDT also has worked wonders for farmers. Its use has controlled many major insect pests, notably those those troublesome to cotton, vegetables, and fruit.

Few food-producing areas are free of DDT contamination. There has been awareness of this for some years. The President's Science Advisory Committee in 1963 called attention to low-level contamination of the environment with DDT. As long as two decades ago, DDT residues in milk caused restriction to be placed on its use for controlling flies and other insects on dairy cattle.

Use of certain other organochlorines on forage grazed by dairy cattle was restricted for the same reason; namely, residues in milk.

Use of DDT in the United States during crop year 1970 was only 33 percent as much as in 1959. Its use peaked in 1959 at more than 78 million pounds but declined to less than 33 million in 1968, 31 million in 1969 and 26 million in 1970. Current plans, barring cancellation, call for reducing DDT usage on cotton significantly in the next few years through pest management programs involving scouting, use of biological and cultural controls, and other other measures.

Much of the contamination from persistent pesticides may have resulted from excessive use. Although environmental contamination from past usage will

continue for a period of years in lessening amounts, further reduction in usage and careful application of all pesticides can be expected to substantially lessen this type of pollution of the environment.

Progress with less hazardous controls. Research has already developed chemicals suitable for use to control many target pests and which are less persistent and more specific than the organochlorine insecticides. Readily degradable chemicals and biological, physical, and cultural controls as an integrated assault offer areas for research into possible answers to many uses of persistent pesticides. The emphasis on newer weapons includes the study and development of viruses causing insect diseases, sterilization of adult insects to disrupt their reproductive cycle, synthesis of natural insect attractants or effective substitutes as lures, ultraviolet light and ultrasonic sound as control agents, hormones that interfere with normal insect growth, and the manipulation of genes. Further research is being stimulated in the breeding and utilization of domestic and imported predatory and parasitic insects, long used as essential biological aids in the control of a number of insect pests. Application of new technology and increased acceptance and adoption of pest management principles and practices should enable us to reduce pesticide use significantly. On cotton, for example, if projected plans materialize, it is anticipated that a reduction in the use of DDT from 10 million pounds in 1972 to about 2 million pounds in 1975 can be effected. To say the least, the future will be challenging and perhaps wrought with some frustrations.

So far, I haven't said much about safety as it relates to the use of pesticides. Our safety records are good, but we hope they can be improved in the years ahead. Pending legislation, stricter enforcement of existing laws and regulations, and the Occupational Health and Safety Act of 1970 should be of material assistance in helping decrease accidents and fatalities associated with pesticides. Plans also call for stepping up educational work with audiences such as dealers, applicators, and farm workers in the years ahead. Some of these audiences are likely to be more receptive because of the legal implications, possible licensing requirements, record-keeping requirements, use restrictions, and other aspects.

Future emphasis on pesticide safety will be directed to supervisors and workers who are involved in operations related to the use, record-keeping, storage, handling, transporting, mixing, and disposal of pesticides. Another area which will be given added attention is that of selection and use of safety equipment, clothing, sanitation, and personal hygiene. Implementation of work in this latter area is expected to be effected through cooperative efforts on the part of the medical profession, public health officials, industry and educational groups.

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INTRODUCTION TO THE CHEMICAL ANALYSIS OF PESTICIDES

A. Curley

In pesticide analysis at the trace level the proper collection, preservation and storage of samples are extremely important. To insure meaningful analysis, the samples should be preserved and shipped to the chemist without degradation and contamination with impurities that might interfere during analysis. For tissues, wide mouth glass bottles with screw caps containing foil liners are recommended. Glass vials with foil-lined screw caps are recommended for blood samples. Tissues should be deep frozen (-12 to -18°C) until time of analysis or held at normal refrigeration temperature if the analysis is immediate or within 24 hours.

Since most samples in pesticides health effects research are animal tissues and excretia, this discussion will be limited to those methods used to assay samples for pesticides as the parent compound and its metabolites. The epidemiological investigation will usually provide the analyst with some information about the possible contaminant. Based on the available samples, he can then make a decision on the behavior of the chemical in various methods and then make the proper selection of the method that will be used for analysis.

For fatty samples, the multiresidue extraction and cleanup method involves extraction of fats and pesticides with petroleum ether, acetonitrile partitioning, dilution of acetonitrile with water and extraction into petroleum ether, florisil column cleanup, partition chromatography and any supplemental cleanup (modified Mills, Onley and Gaither procedure). Non-fatty samples may be extracted with acetonitrile or water-acetonitrile. The acetonitrile is diluted with water and the pesticide residues are extracted into petroleum ether followed by chromatography on a Florisil column eluting with mixed petroleum and ethyl ethers.

Specific methods for the analysis of chlorinated pesticides are the modified Dale, et. al. hexane extraction procedure for blood and the modified method that combines portions of methods by Rivers and by Cranmer and Freal for the determination of pentachlorophenol in blood and urine by extraction of the acidified sample in benzene, methylation with diazomethane and subsequent analysis by electron-capture gas-liquid chromatography either on 4% SE30/6% QF-1 or 5% OV-210. Other chlorinated monophenols, biphenols and chlorophenoxy herbicides can also be analyzed by similar methylation methods.

The pesticide analyst is sometimes required to make assays pertaining to organophosphorus pesticides. In metabolism, oxidative reactions usually result in detoxification of the compound but with organophosphates oxidation can lead to a metabolite that is more toxic than the parent compound. Thus, parathion is converted to paraoxon and systox to sulfoxide and sulfone. Hydrolysis is another detoxification process. Biochemically active compounds or those that are active as a result of metabolism are hydrolyzed by breaking any P-OR or P-SR bond that destroys the actual or potential activity. Multiple detection methods have been devised to analyze (identify and quantitate) the phosphate residue as the parent compound or an altered or metabolic product. Specific methods have been devised to detect the phosphate residue in urine as hydrolysis products - phenols from parathion and salts of dimethyl or diethyl phosphates, thio and dithiophosphates. Sensitive procedures have been devised to measure the cholinesterase activity of these compounds.

Gas-liquid chromatography is usually used for quantitative determinations of chlorinated, phosphorous and nitrogen-containing pesticides in residue analysis. The detection system utilized depends on the structure of the compound or the functionality present in the molecules. This system can be either electron-capture, electrolytic-conductometric, microcuolometric, thermionic, flame photometric or thermal conductometric. Individual pesticides may be detected by one or more detectors but they may not be recovered through the recommended extraction and cleanup procedures as previously discussed. This technique utilizing the most sensitive detection system, i.e., electron-capture, can identify and measure subnanogram amounts or a few parts per billion of a compound. The basic instrument consists of an injection port, column packed with a support coated material, a carrier gas supply and regulators, a detector and an electrometer and recorder to amplify and record the detector signal, including associated equipment such as temperature regulators. Presently, there is a large variety of commercial sources for various gas chromatographs. Good chromatograms with low signal-to-noise ratios and stable baselines are important for meaningful interpretation of the curves.

Column selection, like detectors, must be based on the class or functionality of the individual pesticides. Glass columns are recommended for most pesticide analysis. Pre-coated packing materials can be bought commercially; however, the liquid phases and solid supports can be bought separately and the columns prepared by the laboratory staff with excellent efficiency. Columns are made ready for use by heat curing, silylation and pesticide conditioning. Column efficiency is usually referred to in terms of the number of theoretical plates because of the similarity of a gas chromatographic column to a distillation column. The efficiency of the column can be obtained from the chromatogram by the expression $n = 16\left(\frac{rt}{w}\right)^2$.

Where n = number of theoretical plates of a column towards a particular compound.
rt = retention time, retention volume, or corrected retention volume of the same compound.
w = peak width corresponding to the same compound.

Once the number of theoretical plates, n, is known the height equivalent to a theoretical plate, HETP, or H can be calculated by:

$$h = \frac{n}{L}$$

Where n = number of theoretical plates
L = length of column

Columns can be used over long periods of time if properly maintained.

Although non-specific but highly sensitive, the electron-capture detector is the most used in pesticide analysis. This detector is an ionization detector consisting of a cell with polarized electrodes electrically insulated from each other. The radioactive source, usually tritium - a weak beta emitter, produces the ionization of the compound. For a hydrogen flame detector it is the flame itself. The effluent gas from the GLC column passes through the cell to monitor its electrical conductivity. At equilibrium, the conductivity is a constant. Compounds in the effluent carrier gas to which the detector responds changes the conductivity. The changes in conductivity are measured continuously throughout the chromatographic analysis.

A d.c polarizing voltage is usually supplied to the detector, whether electron-capture or flame. If the e.c. detector is used it is important to determine the optimum operating voltage by establishing a background signal profile. As radioactivity decreases from contamination of the detector periodic measurements should be made to provide up-to-date information on the detector performance. For quantitative analysis, the analyst should always be certain that the compound concentration is within the linear range of the detector.

The thermal conductivity, microcoulometric and electrolytic conductometric detectors are non-ionizing detectors. The first two are much less sensitive than the latter. These are relatively specific and can be used for confirmation purposes. The flame photometric and thermionic detectors are used as specific detectors for phosphorus-containing compounds. Sulfur-containing compounds are also determined with the flame phorometric detector.

Thin-layer chromatography is often used for qualitative confirmation of pesticide assays by gas-liquid chromatography; however, the technique can also be used to make semi-quantitative determinations. Aluminum oxide plates (8" x8", 4" x 4" or 1" x 3") are generally used for chlorinated organic residues. The solvent development systems and visualization techniques are as follows:

Development System	Visualization
n-heptane 2% Acetone in n-heptane	Spray with $AgNO_3$ and 2-phenoxyethanol. Expose to UV.
n-heptane 2% Acetone in n-heptane	Incorporate $AgNO_3$ in layer. Expose to UV.
n-heptane 1% Acetone in n-heptane 2,2,4-trimethylpentane with 25% DMF	Spray with $AgNO_3$ and 2-phenoxyethanol. Expose to UV.
n-heptane 2% Acetone in n-heptane	Incorporate $AgNO_3$, dichlorofluorescein and hydroquinone in layer. Expose to UV.

The R_f values represent the migration distance of the pesticide compared to a reference compound. These R_f values for various solvent systems can be effectively used to indicate whether pesticides found by GLC will be separated on the plate and to assist with the identification of the pesticide.

Ionic chlorinated organic residues can be determined by TLC but the developing solvent system is generally changed to a more polar system such as n-hexane saturated with acetonitrile. Organophosphate esters (thio phosphates, non thiophosphates) can be determined by the methods of Kovacs and Watts. The methods of Kovacs and Watts are as follows:

	Development solvent	Chromogenic agent
Kovacs	Methylcyclohexane (15%-20% DMF in ethyl ether dipping solvent)	tetrabromophenolphthalein ethyl ester, $AgNO_3$, citric acid.
Watts	20% methylene chloride in cyclohexane	4-(p-nitrobenzyl) pyridine in acetone.
		10% tetraethylene pentamine in acetone.

The methods of Mitchell and Mills present paper chromatographic techniques for chlorinated organic residues.

Apart from extraction p-value determinations TLC and paper chromatography, spectroscopic methods are currently being used for most confirmatory tests to substantiate GLC analysis.

The most sensitive of these methods is combined gas chromatography mass spectrometry. The instrument consists of a gas chromatograph interfaced through a molecule separator with a mass spectrometer. The molecule separator effects a separation of the organic effluent from the carrier gas. Presently, quadruple instruments and chemical ionization sources are of particular interest. Mass spectrometers have been computerized for ease of data reduction and interpretation. Using a low to medium resolution instrument, unity mass can be obtained with accuracy. High resolution instruments give more accurate mass measurements to millimass units. In either case one gets an accurate estimation of the molecular weight of the compound. If enough sample is available infra-red and ultra-violet analysis can be made to determine the functional groups present in the molecule. These data together with nuclear magnitic resonance spectra for the proton determinations provide a great deal of structural information about a substance that ultimately aids the analyst in making a positive identification of the compound.

The principles involved in IR, UV, and NMR spectroscopy including the mechanics of measurement, applications and tables of data on characteristic absorption of functional groups and correlations of hydrogen bound to carbon can be found in standard texts and monographs. One suggested monograph is "Application of Absorption Spectroscopy of Organic Compounds" by Dyer.

For pesticides containing heavy metals such as the organomercurials, arsenicals and thallates, atomic absorption spectrophotometry has gained widespread use. This technique usually involves the destruction of the sample by wet ashing, chelation and extraction into a suitable organic solvent and analysis by flame photometry. More recently flameless techniques have been developed to analyze mercury. This laboratory is working on a flameless technique for arsenic determinations. These flameless techniques involve suitable reduction of the sample and the generation of a vapor that is passed into a tube that is placed in line with a beam of monochromatic light. If a flame is used, the light is also passed through it, resulting in reduction of its intensity by a portion of light. Since the absorption is proportional to the concentration of neutral atoms in the flame, quantitative determination of the concentration of the metallic element in the original solution can be found by measurement of the absorption. The Beer-Lambert law which states that the intensity of the transmitted light is affected by the concentration of the absorbing species and the thickness or length of the absorbing medium is obeyed in atomic absorption spectrometry. This law may be expressed as:

$$\log \frac{I}{I_o} = -K_\lambda lc$$

or $$\log I = \log I_o - K_\lambda lc$$

where I_o = initial intensity

I = reduced intensity

K_λ = extinction coefficient

l = length of absorbing medium or thickness of flame in AAS

c = concentration

Such topics as the function of the flame, flame temperatures, suggested gases for certain types of burners and specific metals, burner operation, multi-passing optics, recommended hollow cathode lamps, the monochromotor (grating choice and atomic line choice, i.e. primary or secondary) recognition and elimination of interference and flame emission are discussed in detail in technical bulletins or manuals from the manufacturer or in textbooks and the Atomic Absorption Newsletter as published by the Perkin Elmer Corporation.

The elements of primary toxicological interest are mercury (Hg), lead (Pb), thallium (Tl) and arsenic (As). These elements can be determined in the same sample using the chelation - extraction flame technique. Mercury and arsenic can be analyzed by the above or the reduction, flameless technique.

In summary, this brief discussion has presented some aspects of the principles, techniques and applications of those methods and instrumentation that are presently being used for the chemical analysis of pesticides in tissues and excretia of experimental animals and humans. These methods, either modified or in their present form, can also be used for certain environmental samples.

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