An Agromedical Approach to Pesticide Management

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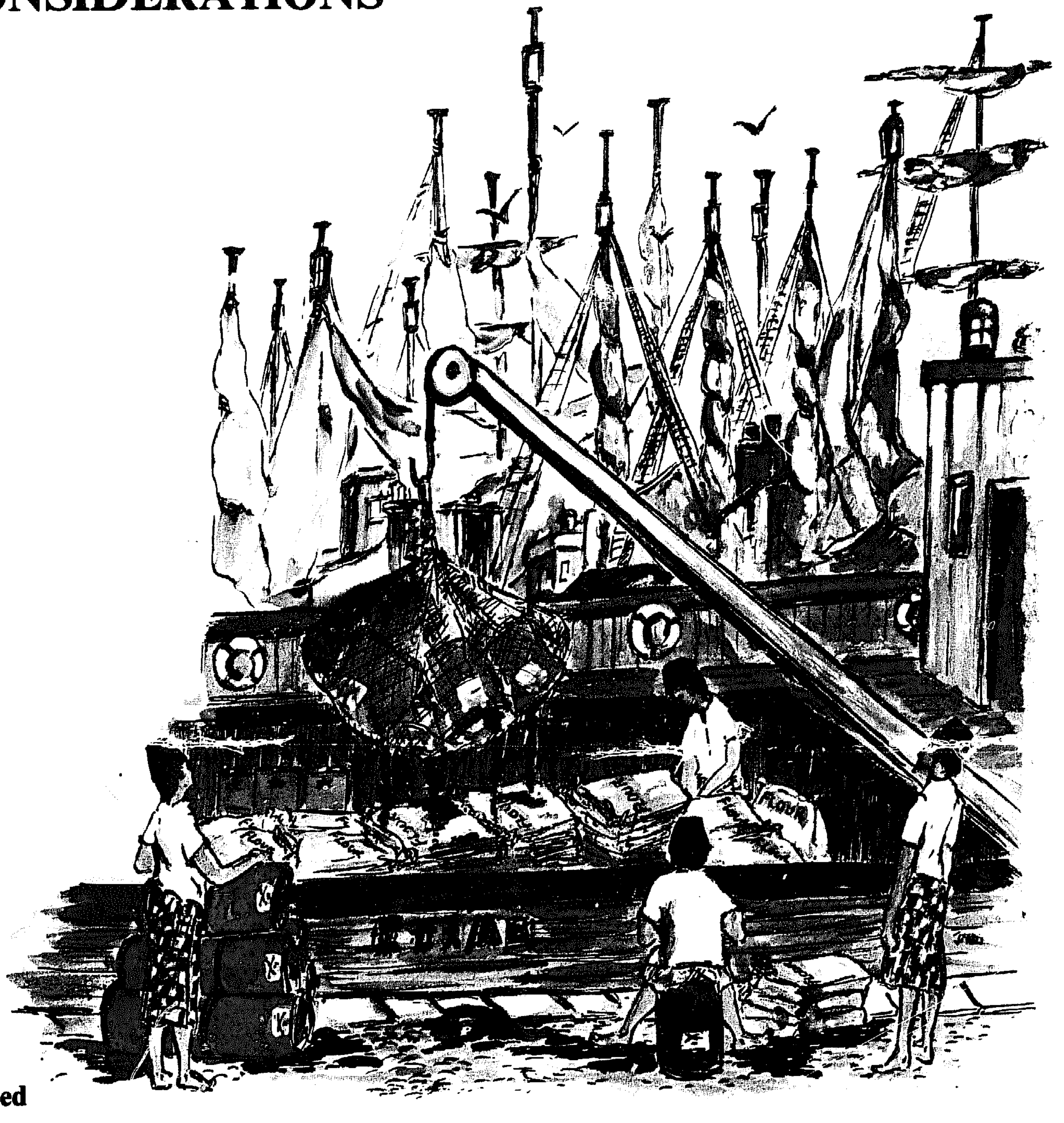

Edited
by

John E. Davies
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PREPARED IN COOPERATION WITH THE:
AGENCY FOR INTERNATIONAL DEVELOPMENT
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AN AGROMEDICAL APPROACH TO PESTICIDE MANAGEMENT

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This book is dedicated to the memory of . . .

LINDA

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International
Crop
Protection**

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There is no intention by the authors to stereotype by sex any health personnel or workers. To avoid a cumbersome text, the words "he" and "she" have been used interchangeably.

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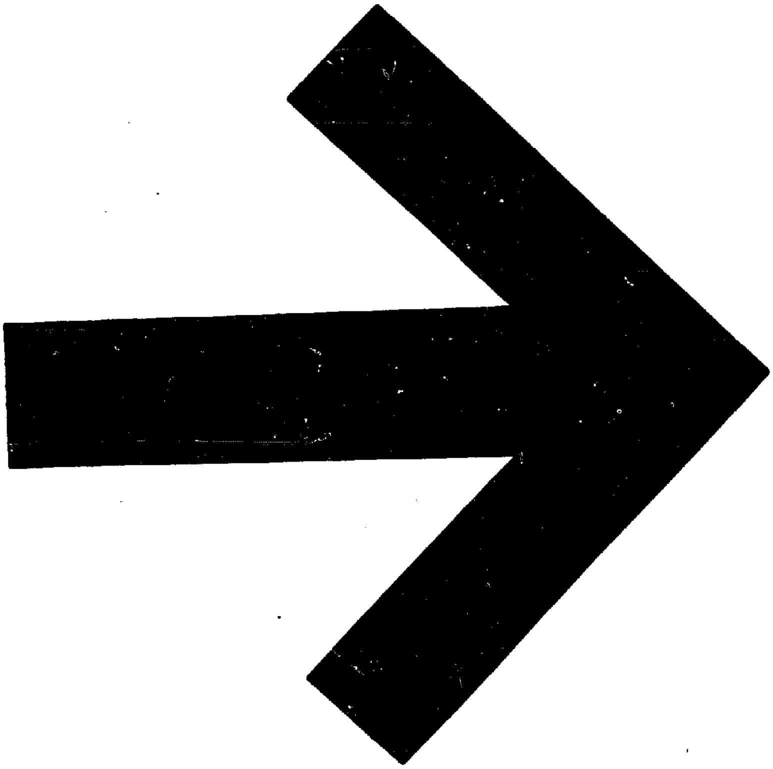

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FOREWORD

This book, the preparation of which was stimulated by experiences gained while working for FAO, WHO and the Consortium for International Crop Protection's A.I.D. Funded Project on Pest Management and Related Environmental Protection over a period of some twenty years, is primarily designed to assist agromedical planners and supervisors of food production and human health programs in the lesser developed countries (L.D.C.'s).

The book has also been designed to assist the lower echelons of the agromedical infrastructure since it is here that the individuals themselves may be directly concerned with adverse health effects caused by pesticides. In the latter context, this book will also serve as a training manual for an expanded "Train the Trainor" program, on general considerations of the agromedical approach and the principles of diagnosis and treatment of pesticide poisoning.

Hence, the book is divided into three Parts:

Part I - The Agromedical Approach - General Considerations

Part II - Prevention, Diagnosis and Treatment of Pesticide Poisonings

Part III - Agriculture, Public Health and Environmental Considerations

Parts I and II were designed to provide background information for trainees in the "Train the Trainor" programs, which are conducted by the project.

Parts I and III are designed to provide background information to participants in the Pesticide Management Seminar/Workshops which are also conducted by the project.

The concept of agromedicine, which is defined and described more fully in the first chapter, is based on the following premises:

> Global malnutrition and starvation are already with us in many parts of the world,
>
> The risk of famine in the years ahead is a very real threat,
>
> The traditional methods of crop protection which have been used by small farms for centuries must be improved by the introduction of socially and economically acceptable appropriate technologies based upon modern agricultural concepts to enable small farms to produce enough high quality food to avoid the impending crisis,
>
> Agricultural pests often produce crop losses of up to 50% if losses incurred during production as well as storage are added together.

Chemical pesticides for the control of agricultural pests and diseases as well as insect vectors of diseases of public health importance will continue to be required for the foreseeable future; although, more and more they will be primarily used as essential components of integrated pest management strategies.

Chemical pesticides are inherently toxic substances to many forms of life and their proper and safe use must be based upon information drawn from a variety of scientific disciplines e.g., medicine, entomology, plant pathology, chemistry and environmental toxicology, to name but a few.

Over the last thirty years the initially highly successful control of pests by chemicals has been replaced by a period where secondary pest management problems have occurred all over the world.

These problems which are of mutual concern for agriculture and health are:

(1) Pest resistance to pesticides,

(2) Human and animal poisonings,

(3) Persistence of certain chemicals, and chronic pesticide exposures (occupational and incidental),

(4) Disposal of pesticide containers as well as disposal of old, outdated stocks of pesticides.

Acute and chronic pesticide exposures can be minimized by training and technological improvements in the manufacture, formulation, application and disposal of pesticides and containers. Both government and private sectors can achieve this goal by working together to provide training, setting standards for pesticide application, labeling and disposal, and establishing a trained infrastructure to utilize this sophisticated technology in the most beneficial manner.

Incidental exposures of populations are another area of public health concern. Incidental exposures should be monitored to document national and international incidences and prevalences, to detect any untoward changes over time and to identify new chemicals which might appear in our ecosystem in the years ahead. The development of insecticide resistance, however, in contrast to human toxicological problems, is a biological phenomenon which is directly related to the persistence of pesticides as well as their spectrum of effectiveness and scope and intensity of use, and can be somewhat ameliorated by operational factors within the control of local officials. Integrated approaches using non-persistent pesticides only when necessary to prevent economic damage appear to offer the most logical strategies for postponing the ultimate spread of this phenomenon.

These problems were the foundation of the agromedical approach; we hope they explain our Chapter titles and the sequence which we have used for developing the agromedical theme--the close inter-relationship which must be established between the medical and agricultural professions to solve problems of mutual interest and concern.

In our presentation and discussion of these topics we have been strongly influenced by our personal observations of global pesticide management difficulties. Also since it is our hope to interest all levels of society which are concerned with the safe use of pesticides including those levels where communication may be difficult, we have added numerous illustrations, from the talented pen of Joan M. Davies.

In the area of clinical management of pesticide poisonings we have attempted to cover the essential clinical and toxicologic features of selected pesticides rather than present a comprehensive treatise on the subject of pesticide toxicology. Here again, we have attempted to highlight the important issues through the inclusion of actual case studies and epidemics of pesticide poisonings encountered during our surveys.

The impact of the stark contrast of competing needs must surely be one of the most vivid impressions encountered in tropical areas. The ever present threat of vector-borne and parasitic diseases, the obvious manifestations of kwashiorkor, marasmus and blindness stand side by side with human and environmental suffering wrought by the very agents used to fight these scourges. It is this tragic paradox, largely the result of inadequate safety technology transfer, which has prompted us to develop this training program.

Pesticide management is concerned with the skills and arts which must be learned and implemented to protect man and his environment from unnecessary and avoidable pesticide exposure. It is concerned with all the links of the chain of pesticide movement through the environment including manufacture, formulation, mixing, application and disposal. The goal is the minimizing of pesticide exposure which results from the agriculture, public health, urban and domestic pest management programs, and to monitor these from time to time.

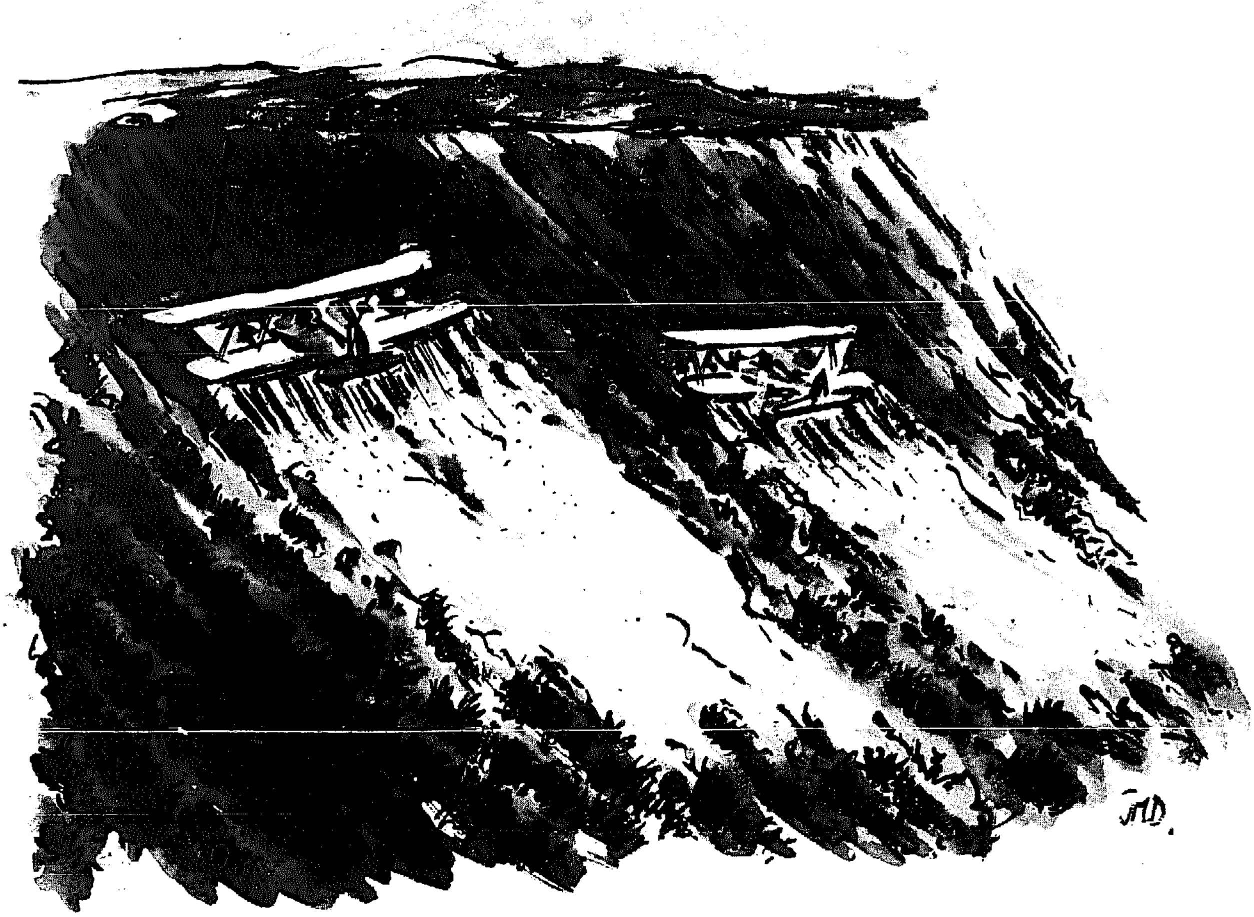
PART I

THE AGROMEDICAL APPROACH TO PESTICIDE MANAGEMENT

Chapter 1

General Considerations

Freed, V.H., Davies, J.E., Smith, R.F. and Whittemore, F.W.



SUMMARY

Human health and agriculture are inextricably related. A balanced nutrition provided by a productive agriculture contributes to the health and well-being of man, improves his resistance to disease, and enhances his capability for productivity. A variety of pests reduce agricultural productivity by as much as 50% or more and are also carriers of human disease. Pest control, therefore, is essential to the well-being of society. Chemicals are extensively used for pest control, but, when improperly used, contribute to both health and environmental problems. An approach called the "Agromedical Approach" has evolved for insuring proper use of pesticides, protection of human health and encouragement of production of agriculture.

INTRODUCTION

Since the title of our manual will be new and its substance may be unfamiliar it is essential that we first review the origins of agromedicine, what is meant by the term and how it relates to pesticide management. Similarly, in light of the significant progress which has been made in the area of crop protection, and integrated approaches to pest management, it is equally important to provide a definition of what we perceive as pesticide management and explain how we believe it relates to pest management.

Background:

The need for medical involvement in pesticide management has evolved over a number of years beginning with the utilization of medical toxicologists in the assessment of the acute and chronic toxicity of DDT, prior to its adoption by the United States Army in 1942. In those early days, however, little if any attention was given to occupational or incidental exposure hazards, nor to possible adverse environmental effects. With the beginnings of the development of resistance to DDT as early as 1948 and the resulting research leading to the discovery of more acutely toxic pesticides, concern with the human health hazards associated with these more toxic compounds resulted in increased involvement of the medical profession, accompanied by a growing concern with the persistence of some of these chemicals and their deleterious effects on the environment. As the use of these pesticides for agricultural purposes expanded after World War II, their extensive use particularly for the control of cotton insects in Central America and India (Chapin et al., 1981) also contributed to the development of resistance of anopheline vectors of malaria as early as 1960. Thus it was becoming readily apparent that the extensive use of pesticides for agricultural purposes under some conditions, was contributing to the problem of the control of human diseases and that a cooperative agromedical approach to the solution of such problems was required.

The need for an agromedical approach to pesticide management was further reinforced when we visited several areas of the world where food production was the single most important ingredient for economic and technologic development.

In the countries that we visited, great efforts were being made to increase and diversify crop production. However, serious pest problems limiting production necessitated crop protection through the use of agricultural chemicals. Although endeavors were highly dedicated and strongly motivated to respond to the national and international needs for food and nutrition, it soon became apparent that ultimate success of these visions in terms of improved food production and economic growth might well be thwarted because of the secondary agricultural and public health problems of pesticide management. These problems can be expected with a technology as sophisticated as pesticide use unless there is a trained infrastructure with capabilities in human safety, and environmental protection.

The twin problems of sufficient food and freedom from illnesses have been a concern of man from time immemorial. These problems continue to this day, and demand a substantial continuing effort to avoid a major catastrophe from either cause. Nutrition and health are inseparable problems. Inadequate food leads to greater susceptibility to many diseases and to a reduced ability to produce. Similarly, many illnesses reduce food assimilation, exacerbating the deterioration of health.

In many regions of the world pests -- insects, weeds, rodents and a host of other organisms -- are largely responsible for the transmission of diseases and the loss and destruction of food. Crops losses of 20 to 30% during production and 20% or more during storage are not at all uncommon. Vector-borne diseases exact a heavy toll of human suffering and death. WHO (World Health Organization), for example, estimates that something over 100 million human beings are afflicted by or will contract malaria. Other tens of millions are under threat of dengue fever, onchocerciasis, schistosomiasis, and other diseases.

These general examples serve to illustrate the importance of the various pests and their enormous impact on human health, food production and welfare. They also indicate why such great energy and effort have been and continue to be devoted to pest management in both public health and agriculture.

The common interest of medicine and agriculture in pest control stems from the shared basic goal of contributing to the health and welfare of humans. While medicine seeks to prevent and cure diseases, agriculture endeavors to provide the food for an adequate and nutritious diet to maintain that health. One without the other is destined to fail. Thus, unwittingly, up until a few years ago each profession pursued its separate interests, particularly with respect to pest control. No longer is this acceptable. The achievement of a healthy productive society is inextricably bound to the simultaneous success of both professions. It is from this fact that the concept of "agro-medicine" sprang, and it will simplify matters if we define what we perceive as the "agromedical" approach to pesticide management (Davies, et al., 1978).

Concepts of the Agromedical Approach to Pesticide Management

Pesticide management is defined as monitoring and regulating or controlling all the links of the chain of pesticide movement through the environment; including manufacture, formulation, transport, mixing, application and disposal. The goal is the minimization of exposure while achieving effective pest management in agricultural, public health, and urban settings. It is also concerned with the need to monitor the use of pesticides on a regular basis to assure both safe and effective use in the overall pest management program. Indeed, without an effective pesticide management program, an efficient pest management program is frequently difficult if not impossible to implement.

Having defined pesticide management, it is easy to understand our concept of agromedicine which is concerned with the integrated interdisciplinary application of the skills and knowledge of agriculture, applied chemistry, and medicine to the safe global production of enough food of high nutritional content to meet the health and nutritionals needs of man.

Such a definition also needs clarification in terms of what it is not. Agromedicine is not merely agricultural medicine, nor it is solely concerned with occupational medicine as related to pesticides. Another consideration inexorably linked with this is the simultaneous protection of the environment. It is therefore, an integrated approach of the several disciplines to safely produce the required amount of the right food for man, and protection from vector-borne diseases. We shall describe later the several pesticide management problems that we have encountered during these earlier visits to several developing nations. The resolution of these problems seems unlikely in the years ahead unless there is a solid and firm integration of the disciplines of agriculture and health.

AGROMEDICAL PESTICIDE MANAGEMENT PROBLEMS

As will be further discussed in Chapter 4, many of the current pesticide management problems stem from one problem which was encountered many years ago and is becoming more important as time goes on, that of pest resistance to pesticides. In attempting to find solutions to this problem i.e. to find pesticides which could be used for the control of resistant pests, a whole host of pesticides, have been introduced onto the world market and are being widely used for both agricultural and public health purposes. Many of these newer pesticides are much more acutely toxic to users than were some of the older pesticides and their use has led directly to three additional pesticide management problems. Hence four of the most important current pesticide management problems are:

1. pest resistance to pesticides
2. human and animal poisoning
3. persistence of certain pesticides resulting in chronic pesticide exposure (occupational and incidental)
4. disposal of pesticide containers and old, outdated stocks of pesticides.

Problem 1. Pest resistance to pesticides.

In the period prior to World War II, various botanicals such as nicotine, derris and pyrethrum and inorganic chemicals such as sulfur, arsenicals and fluorides as well as soap and miscible oils were in common use for plant protection chemicals (Martin, 1940). Although some resistance problems were encountered during this period they were not of significant importance except in some widely scattered instances. While both DDT and BHC were discovered and widely used for military purposes during World War II it was not until the wide scale use of DDT and BHC in the immediate post World War II period, that serious resistance problems began to emerge. The discovery of DDT and BHC also, led to the discovery of a number of other pesticides derived from the chlorination of hydrocarbons, such as aldrin, dieldrin, chlordane and heptachlor. Many of these pesticides had relatively low mammalian toxicities, were persistent and had a wide spectrum of effectiveness, properties which, during that period, were considered to be highly desirable. During World War II also, the Germans (Dr. Gerhard Schrader and his colleagues in Farbenfabriken Bayer A.G.) (Martin, 1971) discovered the insecticidal properties of the organophosphates and three of these materials TEPP, parathion and schradan, despite their high mammalian toxicities were subsequently used on a worldwide scale (Smith et al., 1973).

Malaria resurgence due to interface of agricultural and public health management. The vector now bites outside.

Although the carbamates had been investigated for a number of years by the Swiss, the first highly successful one was carbaryl which appeared in the late 1950's (Martin, 1971).

By 1948, housefly resistance to DDT had developed in both Italy, Sardinia and the United States and by 1949, DDT-resistant mosquitoes had been found in the United States (Patton and Whittemore, 1950). From these small beginnings, the resistance problem increased by leaps and bounds, Brown (1961) reporting that since 1945 the total number of species with resistant strains had risen to 137 about equally divided between pests of agricultural and medical/veterinary importance. By 1965, the results of a world survey of resistance of agricultural pests including insects, mites, plant pathogens and rodents indicated that strains of some 200 species had become resistant (FAO, 1965). By 1980 resistant strains of some 414 arthropod pests, 152 of medical importance and 262 of agricultural importance (Georghiou, 1980) had been noted.

In attempting to deal with this ever increasing problem of pest resistance to pesticides, a multitude of organochlorine, organophosphate and carbamate pesticides have been developed and marketed. A number of them are much more acutely toxic than DDT, thus directly contributing to the other three problems of pesticide management.

Problem 2. Human and Animal Poisonings.

As agriculture and public health have switched from the organochlorine to organophosphate and carbamate insecticides, human pesticide poisonings have become a problem on a worldwide basis. Furthermore, it is only too apparent from the paucity of poison statistics that this is a problem whose magnitude is still not fully known. In many areas of the world, acute pesticide related illnesses are often unrecognized and universally under-reported.

Human poisoning - The second agromedical problem

In a review of global pesticide safety, Dr. John Copplestone discusses this problem and provides the World Health Organization estimates of the magnitude of the problem. In 1972, the WHO Expert Committee on the Safe Use of Pesticides considered a mathematical model based on the accidental poisoning statistics for 19 countries. The data indicated that there were as many as 500,000 pesticide poisoning cases annually with a mortality rate of 1% in those countries where medical treatment and antidotes were readily available. In other countries, where resuscitative methods were less available, fatalities were presumably higher (WHO, Tech. Rpt., 1973).

Subsequent to this original estimate of worldwide pesticide poisoning statistics and because of the sizable limits of error of these earlier estimates, the Director General of WHO requested notification of pesticide poisoning cases and deaths in 1974 from all participating countries. Regrettably, many countries reported back there there were no statistics for their country. In one series of reports from five countries, in those countries that did reply, the poisoning rate was 2.9 per 100,000 with a death rate of 1.7 per million the deaths being 5.9% of the cases. In another survey of four countries (Rumania, Syria, Turkey and United Kingdom) the death rate was 5.5 per million of deaths and 4.8 cases per 100,000. Based on the combined death rates of groups 1 and 2, the number of deaths annually may be as high as 20,640 (4,000 x 5.16) (Copplestone, et al. 1977).

Table 1-1. World Health Organization survey of pesticide poisoning incidence and mortality from respondent countries, 1974.

Year	Country	Cases per 100,000	Deaths per Million
1972	Cyprus	2.3	3.1
1974	Finland	2.8	3.4
1974	Ireland	4.6	0.6
1974	Israel	1.6	
1972	West Samoa	6.8	
1974	Rumania	13.0	14.4
1971	Syria	16.3	25.6
1974	Turkey	4.3	4.0
1973	United Kingdom	0.2	0.3

The exact magnitude of the problem in the Caribbean and Central America is unknown but poisoning cases occurring in two Central American countries, El Salvador with 4,387 poisonings and 27 deaths and Guatemala with 4,022 poisoning incidents and 4 deaths have been reported.

In addition to the public health problems of acute pesticide poisonings, epidemiologic studies over the last decade have demonstrated association of <u>occupational exposure</u> to individual pesticides with a wide variety of diseases ranging in severity and diversity from chloracne to cancer. Also, both hypertension and hyperlipoproteinemia were noted in pesticide workers with elevated serum organochlorine levels. Soft tissue sarcomas and histocytic lymphomas were associated with the use of phenoxy acetic acid and and chlorophenol herbicides in Swedish railroad workers and have also been noted in other studies. Neurologic and behavioral abnormalities were noted as a result of occupational exposure to chlordecone, delayed neurotoxicity with leptophos and male sterility with dibromochloropropane (DBCP). These are but a few of the important findings of recent epidemiologic studies into the health effects of occupational exposure to a single pesticide.

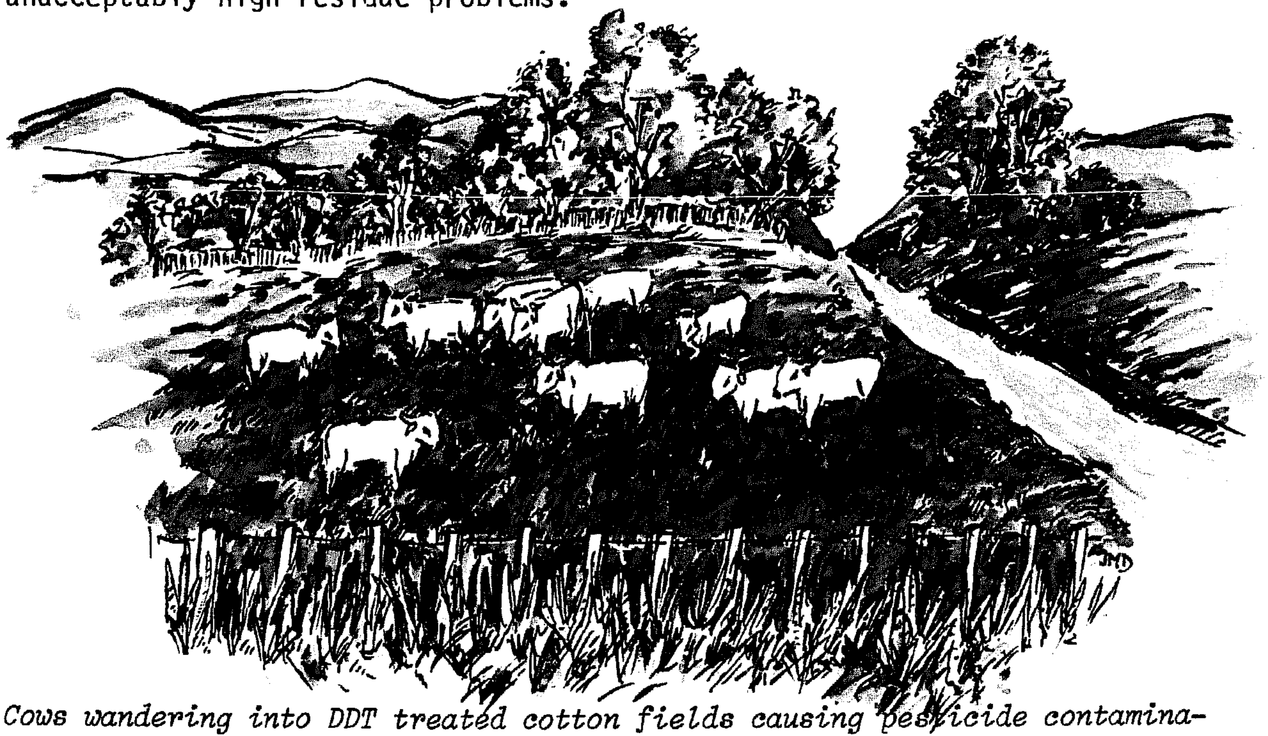
Findings such as these have emphasized the significance of chronic as well as acute pesticide exposure, and not only highlight the need for additional research on human exposure assessment but also the simultaneous requirements for minimizing human pesticide exposure wherever possible. These acute and chronic health effects are further discussed in Chapter 3.

Problem 3. Persistence of Certain Pesticides

Persistence is the third management problem and was highlighted in Central America where serious contamination was recognized in 1974-75. DDT, dieldrin and toxaphene were organochlorine pesticides still widely used in agriculture, particularly cotton production, in Central America; their use in this area has led to contamination of food, and the environment, and posed a serious economic threat to the meat industry. For the most part, pesticides are aerially applied to cotton later in the season, thus, the crops there not only acquired a residue, but the drift contaminated adjoining pasture lands which subsequently contaminated any cattle that would graze there. Moreover in some areas it was common practice to pasture the cattle on the stalks following harvest. Cattle fattening in pens were fed seed meal contaminated with DDT. Cotton seed oil, which had been treated with dieldrin, was used for fattening purposes. These several practices led to significant contamination of cattle meat from grazing and from foodstuff sources (Pest Control & Public Health, Vol. 5, 1976).

Verification of significant contamination of milk, meat, fish and wildlife was demonstrated by an ICAITI survey. Residues of DDT and its metobolites in milk ranged from 2-63 ppm, and residues of this pesticide and its metabolites in meat ranged from 0.81-24.5 ppm. Dieldrin residues in meat and milk ranged from 0-1.0 ppm (ICAITI, 1976).

Since 1976, the picture has not changed appreciably. A significant number of the world's cattle are raised on the pastures of Central America. As a result of the contamination described, significant economic losses have ensued, with more than $1.5 million being lost by the beef industry. With residues of these orders of magnitude, concern has been expressed for human health consequences from the ingestion of contaminated meat. This concern is appropriate in the absence of significant human monitoring for pesticide residues. The cattle industry in these areas is still plagued with unacceptably high residue problems.



Cows wandering into DDT treated cotton fields causing pesticide contamination of milk and meat. Persistence - the third agromedical problem.

Problem 4. Disposal of Pesticide Containers and Old Out-dated Stocks of Pesticides

Proper disposal of pesticide containers, particularly if they are made of metal, fibreboard or plastic, is an urgent problem in many LDC's where there is a container shortage. On many occasions we have seen them being used to store or carry a variety of materials including food and water; likewise the polyethylene liners of fibreboard containers are often used as improvised raincoats in the humid tropics. On the other hand we have frequently encountered instances where rural (and urban) storekeepers dispense small quantities of various pesticides in unlabeled bottles or paper bags. Once the pesticide concentrate has been transferred from the original container to these small, unlabeled soft drink or used beer bottles the necessary ingredients for an accident are all in place.

Situations where old and outdated stocks of pesticides are either stored in the open or in completely inadequate storage facilities are frequently encountered. The problem is further compounded by the fact that in many instances, the labels have been defaced or lost so that neither the active ingredients nor the suitability of the product for its intended use can be readily determined.

The problem will be further discussed in Chapter 15, Transport, Storage and Disposal of Pesticides.

Ingredients of the Agromedical Approach to Pesticide Management

Historical Development

The recognition of the urgent need for an agromedical partnership in the area of pesticide management has long been recognized. Dr. Julie Sulianti Saroso, the Minister of Health in Indonesia in 1969, was one of the earliest advocates of a close working relationship between the Ministries of Health and Agriculture especially in the area of pesticide management. The risks and benefits of agricultural chemicals had become an especially important issue in that part of the world because of the continued public health problems of vector-borne diseases such as malaria, dengue fever, and filariasis. The early development of anopheline resistance to DDT and dieldrin in different parts of Central Java stimulated the switch to the organophosphate insecticides, a change which agriculture also made because of the emergence of insect resistance in the major agricultural pests. During this time, partly because of the switch to the organophosphates, pesticide poisonings soon became a significant public health problem, and several consultants were sent by the World Health Organization to this part of the world in order to document, and verify the health-related effects of pesticides (Davies, 1969 and 1974).

Later, Dr. Iwan Darmansjah of Indonesia, reviewed some of the problems of pesticide management and safety programs in Southeast Asia. He described how his country approached the pesticide poisoning problem with the idea of the development of pesticide protection teams. These materialized during the period of 1970 to 1973. Such teams consisted of a medical doctor trained in epidemiology and agromedical problems, a pharmacist or a chemist in charge of a modest laboratory possessing the capability of cholinesterase and thin-layer chromatography determinations, and a sanitarian conversant in public health activities. Close collaboration of these units with agriculture was implemented and the program was first developed in 12 of the 26 provinces.

Since 1974 pesticide protection teams have been operational in all 26 provinces reporting into a "Central Health Team" supervised by the "Surveillance Unit" of the Department of Health in Djakarta. Such an organization representing three key disciplines of agromedicine and possessing a peripheral infrastructure tied into a "Central Surveillance Unit" was the first of its kind. The major responsibilities of these "Provincial Pesticide Protection Teams" were to establish a chain of command for environmental training, particularly in the area of agricultural chemicals and the establishment of an interdisciplinary unit capable of scene investigation and chemical verification of episodes thought to be related to human and environmental pollution and poisoning due to pesticides. Darmansjah also states, "that additional training programs in agromedicine for agricultural uses of pesticides are provided by the Agricultural Extension Services in Southeast Asia, even in those countries having no pesticide regulations." (Darmansjah, 1973).

In the U.S. at about the same time, the HEW "Secretary's Commission on Pesticides and Their Relationship to Environmental Health" concluded its deliberations on the topic, reporting to the Secretary of the United States Department of Health, Education and Welfare on the risks and benefits of pesticides. In this report which was published on December 5, 1969, the fourteen recommendations included: Recommendation 9 which advised the Secretary to establish a Department of Health, Education Welfare clearing house for pesticide information and the development of a pesticide protection teams.

The recommendation called for the establishment of a clearing house for pesticides, and the organization of pesticide protection teams was strongly urged. It stated that "The clearing house should:

- ° Collect and organize information on pesticides and their relationships to human health and the quality of the environment in a modern system for storage, retrieval, dissemination, and secure evaluations of such data.

- ° Provide bibliographies, reprints, and summaries upon request from the Secretary of the Department of Public Health, Education and Welfare, appropriate Federal and State agencies, research centers and others with a valid need for knowledge.

- ° Receive continuously information from the pesticide protection teams and provide for its proper summary and distribution, with special attention to dangers or improvements related to methods of pest control.

- ° Maintain liaison with national and international bodies active in the field of pesticide safety.

- ° Receive, summarize, and distribute data from pesticide monitoring programs relating to human health and welfare.

Pesticide protection teams should be developed from existing local personnel and coordinated with Federal and State personnel and facilities from agriculture, wildlife, and public health. They would:

- Augment existing agricultural extension, and fish and wildlife efforts relating to pesticides and thereby guide local usage and safeguards.
- Improve local surveillance of pesticide contamination, facilitate monitoring of human tissue residues of pesticides, and investigate usage patterns and episodes of human toxicity.
- Provide a rapid flow of local information based on the above activities, to and from the clearinghouse, especially concerning any emergency relating to pesticides.
- Inform the public, users of pesticides, local governments, and enforcement agencies on techniques for disposal and other matters.
- Stimulate local awareness and constructive concern essential for optimal use of pesticides." (Report of the Secretary's Commission on Pesticides, 1969).

Thus, in two different parts of the world, the one a developing and the other a developed nation, both with considerable and costly experience in the risks and benefits related to the use of pesticides, advocated a closer agromedical partnership as a solution to these problems.

Current Concepts

The essential ingredients recommended by these two reviews from Indonesia and from the United States emphasized the necessity of an interdisciplinary network of personnel skilled in public health, chemistry and agriculture. The organization envisioned would include a central clearinghouse with an infrastructure radiating throughout the nation. The responsibilities would be to investigate alleged insults affecting human health and the environment from agricultural chemicals and verifying the same by scene investigation and appropriate laboratory testing. This information would be reported to the central clearinghouse. Finally, such an agromedical organization should improve the technology for safer, more effective use, and provide continuing training of agricultural and health personnel in these areas.

As the use of agricultural chemicals increased in the following years, especially in the Third World, pesticide management problems increased so that there was soon widespread recognition of the need for pesticide safety for the protection of human health and the integrity of the natural environment. This trend could be identified in most of the nations seeking economic development based upon an increase of cash and food crops.

The need for training in pesticide safety and use resulted in the development of a project entitled "Pest Management and Related Environmental Protection" funded by US/AID to the University of California, Berkeley, California. The purpose and the role of this project was to review the problems of pest management and pesticides in different areas of the world, and provide technical assistance for solution of the problems. Workshops were conducted in such diverse areas as El Salvador, Indonesia, Costa Rica, the Philippines, and Egypt, at which workshop scientists in the fields of agriculture and chemistry interacted with those from medicine and public health with the expressed purpose of developing and expanding the agromedical team approach of pesticide management. The essential ingredients for such a program have become those first advocated by the Ministry of Health in Indonesia and those contained in Recommendation Number 9 in the Report of the Secretary's Commission on Pesticides and Environmental Health.

CONCLUSION

From the foregoing ideas and proposals for pesticide management evolved the more refined concept of the "Agromedical Approach" and development of a "team" or organization for this activity. As conceptualized, the agro-medical approach would deal with pesticide management beginning with the importation or manufacture through formulation, distribution and storage, to the use of chemicals and disposal of containers and unwanted materials. The plans for such an agromedical team in a country would need to be sufficiently flexible as to allow adaptation to governmental structure, customs, and available resources. The idea, however, is to provide an organization that has the capability of affording protection of human health and the environment while at the same time, fostering the production of food and cash crops essential to the welfare of the country. It would be an organization that draws widely on information available in the world literature and from other countries and through careful analysis and synthesis applies that information to the local conditions. Beyond that, the agromedical team would devise the appropriate technology for implementation of laws and regulations, the monitoring of the chemicals used, how they are used, and their interface with human health, and the environment.

The judicious planning fostered by the agromedical approach results in the most prudent use of both human and monetary resources to achieve the greatest benefit. Thus, a system to provide first response in terms of implementation of regulations or responding to health problems, would utilize just the resources needed rather than establishing an elaborate and costly capability. This initial response capability would then be backed up by increasingly sophisticated capabilities that would have the capacity to provide assistance to handle a number of the first response units. In this manner, the greatest benefit is achieved with the least expenditure of resources. Such systems are in the process of development in several countries. Some specific illustrations of alternate approaches in the agromedical system will be discussed in Chapter 21.

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Chapter 2

What Are Pesticides and How They Are Used?

Freed, V.H.

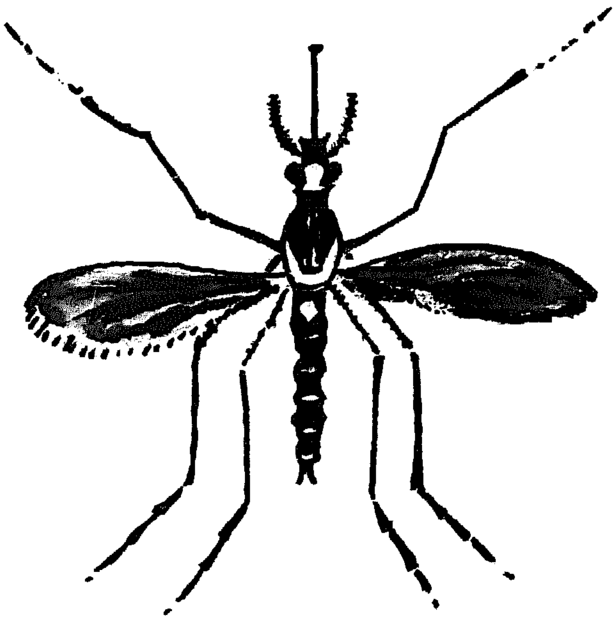
SUMMARY

The purpose of this chapter is to introduce the reader to the types of chemicals used as pesticides. The chemicals are prepared in various formulations--dusts, granulars, liquids, two types of emulsifiable liquids, etc. The toxicity of a chemical depends not only upon its innate properties, but also on the manner and amount used. The effects (if any) produced are a function of the dose-response relationship. Hazards with chemicals can be minimized by a knowledge of what is involved and by taking the proper protective measures.

The types of chemicals used as pesticides are illustrated in this chapter. The chemical and physical properties as they relate to the behavior in the environment and toxicity are briefly described. Thus, knowing such properties as vapor pressure, water solubility and reactivity becomes a basis for predicting adsorption by soil and other surfaces, the escape of the chemical as a vapor, and the possible bioaccumulation. The quantitative relationships that have been developed are briefly described and the application indicated. This information when properly used enables one to predict the probable behavior of the compound in the environment, where it is likely to accumulate, and to deduce the proper methods of formulation, application and use so as to achieve the safest and most effective utilization.

INTRODUCTION

Humans from the beginning of time have been victimized by other species. When it wasn't some carnivore preying on man, it might be another mammal, insect, plant disease, or a plant itself competing for man's food and fiber. If this were not a grim enough situation, mankind became the host to a variety of diseases, and particularly serious were the vector-borne diseases. Archeologists tell us that in excavations dating back some 10,000 years, they found evidence that humans were victims of malaria and similar insect-borne diseases.


Disease Carrying Mosquito

Famines, both local and regional with attendant starvation, have resulted from insect and plant disease attacks from earliest times. Since the time the human race first began to practice any form of agriculture there has been the constant and very real threat of crop loss due to insects, rodents, plant disease, and weed competition. To add to the woes, insects and rodents caused loss of stored crops as did plant diseases, e.g. ergot, or livestock poisoned by plants (Hayes, 1975; White-Stevens, 1971, 1977).

It is no wonder then that as knowledge and understanding increased, attempts were made to devise health and agricultural practices to overcome these threats to the welfare of man. Animal power was substituted for human labor to produce more crops thereby offsetting losses, improved varieties were selected and implements devised for more effective crop culture. A lore of animal medicine emerged as people attempted to protect their livestock from poisoning and disease.


The Hungry Rat

A SEARCH FOR THE PROTECTIVE ELIXIR

Sometime in the distant past, an astute observer noted that concoctions of certain plants or preparation of particular salts would ameliorate the effect of diseases of man. Out of that grew folk medicine and probably from it stemmed the concept of abating the ravages of various pests by means of chemicals. The records indicate that even before 1000 B.C. the Chinese and others had observed that elemental sulfur would protect plants against some of the diseases to which they were subject. Similar observations were made by the Greeks and Romans, but the implementation of those observations was very limited. Likewise, colonists in North America noted that their native plant, tobacco offered a measure of control for certain plant-eating insects as early as the 18th century.

Molds Destroy Food and Plants

Little was done with these sporadic observations of the ability of chemicals to control pests until the 19th century. This despite the fact that for many centuries, the physician used a variety of chemicals to treat patients--albeit with variable success (Hayes, 1975; Sheets and Pimentel, 1979; White-Stevens, 1977).

By the mid-19th century the various sciences began to emerge and with them more systematic studies on effects of chemicals on living organisms. It was found that such materials as sulfur, copper salts, and even sodium chloride, would control plant diseases such as the smut of grain. Subsequently, it was observed that certain compounds e.g. carbon disulphide, chlorinated alkanes, such as chloroform and hydrocarbons, would kill the insects in stored grain. Ultimately, it was observed that certain preparations of copper controlled mildew on grapes and that soluble copper salts would kill broadleaf weeds.

From about 1890 onward there was growing effort to find chemicals that would control vectors of human diseases, insects attacking crops and livestock, and weeds. Most of the materials used at this time were simple inorganic compounds such as copper salts, lead, or calcium arsenate, or sodium fluosilicate. A few organic compounds then available were tried but it remained for the development of the field of organic chemistry to provide the effective pesticides that are available today.

Controlling Weeds by Hand

By the 1930s, large industries were being built around the discoveries of organic chemistry. Among the products that developed in the organic laboratories were chemicals that were proving to be effective for control of insects, plant diseases, and weeds that had long plagued man. Came then World War II with its devastation of the food production and health protection systems resulting in an urgent need for food to prevent starvation. From research laboratories came the safe (low mammalian toxicity) and effective insecticide, DDT, and the dramatically efficacious phenoxyacetic acid herbicides. These contributed significantly to both health protection and food production thus averting the catastrophe of starvation and disease epidemics so often an aftermath of war. The successes with these chemicals stimulated worldwide interest in the development and use of pesticides. The lack of prior experience with such wide-scale use of chemicals in the environment and the ease with which a pesticide could be used sometimes led to an overuse of the chemicals. It was only as some of the adverse impacts such as effects on non-target organisms and later, possible effects on humans (Wagner, 1981) were observed that concern was felt for a more rational use of these essential tools. Subsequently a large variety of chemicals were developed for pest control (Cremlyn, 1979; Green, et al., 1977; Hayes, 1975).

Weeds Choke Out Crops

Today much greater attention is being given to proper use of chemicals in pest management. Currently there is great interest in a system of pest management called "Intergrated Pest Management" or "Integrated Pest Control" which employs all available tactics including chemicals for management of the pests. It should be noted that, in most instances, chemicals are the base of the integrated pest management scheme but used in such a manner as to be compatible with other tactics and avoid adverse impacts.

To many, the action of the chemical on a living organism appears to be a mysterious process. They themselves may use a variety of chemicals in their daily living, some of which may be quite toxic, there is a tendency to feel that any chemical if given in a sufficiently large dose in the proper manner may be harmful. This fact was known to physicians and chemists as early as the 16th century, but seems not to have become part of the general knowledge. Even chemicals comprising our food, if given in a large enough dose, may be as harmful. Thus, any chemical, either natural or synthetic, if abused by ingesting overdoses, can cause either acute or chronic toxicity (Hayes, 1975; Wagner, 1981).

In dealing with the effects of chemicals on living organisms it has been found convenient to categorize the effects into acute, subacute and chronic. The acute effects are those brought on by a sufficiently high dose in

Table 2-1. Classification of Some Common Pesticides

Common Name	Use Classification	Chemical Classification
Carbaryl	Insecticide	Carbamate
DDT	Insecticide	Chlorinated hydrocarbon
Lead arsenate	Insecticide	Inorganic
Nicotine	Insecticide	Botanical
Parathion	Insecticide	Organophosphorus
Atrazine	Herbicide	Triazine
Dalapon	Herbicide	Alkanoic acid
IPC	Herbicide	Carbamate
2,4,5-T	Herbicide	Phenoxy acid
Chloranil	Fungicide	Quinone
Maneb	Fungicide	Dithiocarbamate
PCNB	Fungicide	Nitrobenzene
Compound 1080	Rodenticide	Alkanoic acid
DEF	Defoliant	Organophosphorus
4-CPA	Plant growth regulator	Phenoxy acid
Telone	Nematicide	Chlorinated hydrocarbon

Table 2-2. Major Chemical Classes of Pesticides

Insecticides	Herbicides	Fungicides
Botanicals	Aliphatic acids	Antibiotics
Carbamates	Anilides	Hydrosulfimines
Halogenated hydrocarbons	Aromatic acids	Inorganics
Organophosphorus	Arsenicals	Nitrobenzenes
Thiocyanates	Nitroanilines	Organo-mercurials
	Phenols	Quinones
	Phenoxy acids	
	Pyridiniums	
	Triazines	
	Ureas	

in a matter of a few hours to a day or so. These effects are usually intense and immediately perceptible. The subacute effects are produced by a lower dose and require a somewhat longer time before they are noted. Generally, the acute and subacute effects will be overt poisoning evidenced by a number of symptoms such as nausea, sweating, miosis, salivation, dyspnea, unconsciousness and of course, in more extreme cases, death. Chronic toxicity however, is more subtle and is usually produced by long-term low-level exposure to the chemical or chemicals. The effects may not show up as overt toxicity, but rather appear as blood dyscrasia, reproductive difficulties, nervous disorders, or tumors.

In chronic toxicity, the total dose ingested may be equal to or greater than the single dose that causes acute toxicity. The difference is that the organism has established some equilibrium between the amount of chemical taken in and that which has been metabolized and excreted. To be sure in many instances, there will be a deposition of the chemical in certain organs or tissues, e.g. fat, but even in this case, an equilibrium between intake and metabolism/excretion will be established unless either the metabolic pathway or excretory pathway have been impaired. If during the course of time, the exposure is stopped, then the metabolism/excretion will result in elimination of the chemical from the body giving rise to the concept of pharmacodynamic half-life, that is the time required for one half of the administered dose to disappear from the body.

An important principle to be considered in dealing with pesticides or chemicals in general is the distinction between toxicity and the hazard (Wagner, 1981).

The Potential Hazard

The term hazard implies the risk or likelihood of an adverse effect. On the other hand, toxicity is an innate property of the compound and is the potential for harm, but only if several other factors operate simultaneously.

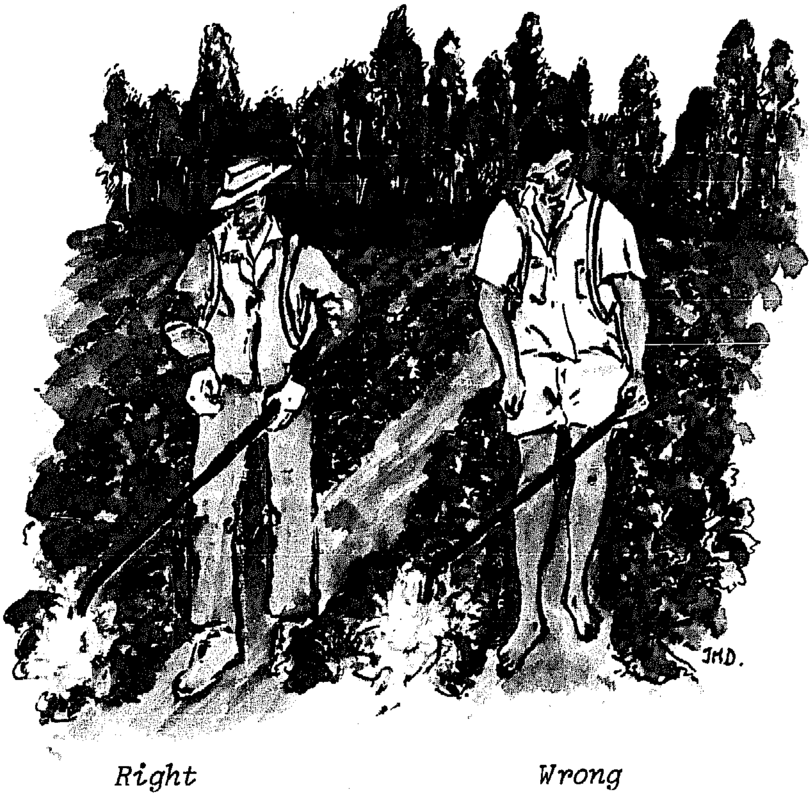
The Actual Hazard

Thus, while toxicity is a singular characteristic of the chemical, the hazard posed involves at least five aspects, namely:

1. innate toxicity of the chemical,
2. spectrum of species affected,
3. the persistence of the chemical,
4. the mobility of the chemical in the system, and
5. the manner of handling and use.

FACTORS AND HAZARD ASSESSMENT

As indicated above, a number of factors should be considered in hazard assessment. Often times some of these factors are ignored and in their stead, tenuous assumptions are employed in the assessment. Obviously in the case of the chemical, if there is no exposure there can be no risk to the organism. However, in the use of pesticides, there is always the likelihood of exposure. Because of many of the effects produced by chemicals follows a dose response relationship, the level of exposure becomes important in hazard assessment. Thus, at very low exposure levels the hazard becomes correspondingly small. One of the factors in exposure is the properties of the chemical. Thus, such properties as solubility, vapor pressure, adsorbability, partition coefficient and the thermodynamic characteristics are important determinants in the level of exposure to which man or other organisms might be subjected during use of the chemical. These properties will influence the extent of vapor contamination of the air, water contamination, biological availability, and persistence of residues. To be sure, the behavior and fate of the chemical while a function of these properties is also influenced by environmental factors, e.g. light, temperature, moisture, etc. Another factor bearing on routes and rates of exposure is the manner of use and the amount used.



Right *Wrong*
Wear Protective Clothing!

A third factor has to do with what precautions and protective measures are employed to minimize the exposure, and hence the risk. Finally, it must be noted that in any given group of chemicals there will be considerable variation in the intensity of biological effects produced, the length of time required to produce them, and the susceptibility of a given organism to a particular chemical.

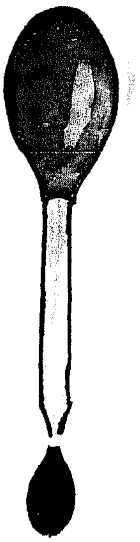
Thus within a group of compounds, one might find one material that is toxic at a very low concentration or dosage level whereas another of the same family of chemicals will have quite a low level of toxicity i.e., require high dosages. Such phenomenon as indicated, is in part attributable to the variability of the properties and geometry of the chemical. While it is hard to quantitate the relationship of some of these properties to biological effects, the phenomenon should be considered in any good risk assessment. For example, among chemicals that have been demonstrated to produce cancer, there are those that upon low dose produce cancers in the test animals, in a very short-term experiment. Other chemicals may require a much higher dose and almost lifetime exposure before cancer is produced. Which then, of these chemicals, poses the most serious risk? It is probable that as we learn more about chemical carcinogens we will discover a broad spectrum of activity ranging from strong carcinogens to very weak ones. There will be compounds that follow the statistical concept of the one-hit theory, but on the other hand we should not be surprised if there are chemicals that will follow a multi-hit model and hence require long-term exposure before the lesion is induced.

Controllable and Uncontrollable Hazards:

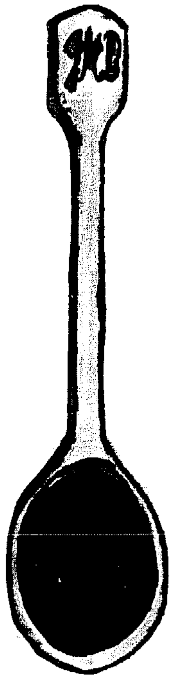
The adverse effects of pesticides, such as acute human poisoning, toxicity to non-target organisms, chronic effects on both humans and environment are often perceived as uncontrollable risks. There seems to be the feeling that because of these effects due to persistence, transport and toxicity, only cessation of use can avoid the risk.

Yet, it was observed as early as the sixteenth century that it is the dose that determines whether or not a chemical will have a toxic effect. More recently in the Secretary's Report (Mrak Commission Report) it was pointed out that it is the manner of use that determines the hazard or probability of toxic effect.

In considering the risks or hazards from use of the chemical, two distinct aspects may be distinguished. Those that are related to the inherent properties and characteristics of the chemical, and those that are determined by the manner of use. The first aspect is that of the properties of the chemical discussed previously.



Just Right



Too Much

The second aspect of risk in the use of pesticide involves those factors that are under the control of man. These include the following:

1. the precautions taken in manufacture, storage and transport,
2. the nature of the formulation--many of the chemical and physical properties can be modified and controlled by proper formulation,
3. the manner of application--proper application can reduce the amount of chemical lost from the target area,
4. the place where used, and
5. the amount of chemical applied in any one continuous area.

Knowing the properties of the chemical and taking steps to apply the controllable factors can substantially reduce the risk of adverse effects on man or the environment. Similarly, the knowledge of these factors and their proper application and the use can reduce the likelihood of the development of resistant varieties of the target organism.

CLASSIFICATION OF PESTICIDES

The classification of pesticides is often confusing to the layman. The chemical may be referred to as an insecticide, herbicide, fungicide, rodenticide or some may say pesticide and herbicide, not realizing that pesticide includes all types of pests. There are two basic schemes of classification one on the basis of use, and the other on the basis of chemical nature.

Since 1945 some 1,500 individual compounds have come into use as pesticides. These chemicals have been offered for sale and application in about 35,000 to 40,000 different formulations. To be sure, only about 150 of those chemicals are very widely used. The remainder are used in smaller quantities or used selectively on specialized problems.

In dealing with the large number of chemicals and the even greater number of different formulations, it would only be natural for one to ask first, "why do we have so many chemicals," and then secondly "how does one keep them all straight?"

With so many compounds and several thousand different formulations, some system of ordering the array of chemicals is needed to properly identify those we wish to use. One scheme is to classify the chemicals by biological use. For example, those used to control insects will be termed insecticides, and those for weed control; herbicides. However, this does not give sufficient identification since a variety of different chemicals may be used for insect control and vary greatly in composition, manner of use, as well as biological and chemical properties. Moreover, we find members of the same class of chemicals being used as both an insecticide, a fungicide and a herbicide as is the case with some of the highly volatile materials designated as fumigants.

Another system of classifying the chemicals is by chemical group. This is somewhat more informative, at least to the chemist, as to the chemical's nature and properties but is uninformative as to whether it controls insects, weeds, or some other pest. Thus, we have aliphatic, alicyclic and aromatic hydrocarbons that are substituted with chlorine, bromine or iodine, all classified as organohalogen pesticides. Further categorization may be made by substituent groups such as carbamic acid esters, phosphates or phosphonates, nitriles, carboxylic acid esters and so on.

The scheme of categorization of pesticides that has evolved is a hybrid between the biological and the chemical classifications. Thus, we speak of organohalogen insecticides, herbicides or fungicides and so on. Such a scheme of classification identifies the chemicals in a generic way as to chemical class and the type of pest controlled. In many cases a sort of "short hand" reference is used. Thus, if we refer to an OP compound, most pesticide control biologists recognize this as containing a phosphorous atom. It also immediately tells them that this is likely to be a cholinesterase inhibiting substance that should be dealt with considerable caution.

Which pesticide?

SPECIFIC CHEMICAL GROUPS

It was easier at an earlier time to categorize chemicals and speak of them as belonging to a particular class for there were fewer chemicals and their structures were such as to make the classification less equivocal. Thus, one could speak of chlorinated hydrocarbons or organohalogen compounds, and generally refer to substances containing carbon, hydrogen and a halogen. As the number and complexity of the compounds increased, the lines of demarcation became less well defined. For purposes of sharper definition of the compounds we are forced to refine the system and utilize subcategories. For example, both DDT and 2,4-D contain carbon, hydrogen and chlorine, but in addition 2,4-D has three atoms of oxygen. We can refer to both compounds as organohalogens, but the DDT is a hydrocarbon, and the 2,4-D an aromatic acid. Even more confusing might be the case of a chemical like Ronnel, an organophosphate containing three chlorine atoms.

Just as there is a continuum in structures of compounds that make some of the classification arbitrary, so there is a continuum in the chemical and physical properties of the compounds. It can be assumed, for example, that a particular property e.g. oil solubility found in one member of class of chemicals will be found in other members of the class and may be found in varying degrees in compounds representative of a different organic class (Haque and Freed, 1975). The following table (Table 2-3) illustrates this point. To illustrate, in the generalized reaction with water, that is hydrolysis, one might deduce that the chlorinated hydrocarbons are resistant to hydrolysis compared to the organophosphates if one considers only DDT. On the other hand, the chlorinated hydrocarbon methyl chloride hydrolizes quite readily. Or yet, again, because of the high fat solubility of many

Table 2-3. Properties of Some Commonly Used Chemicals

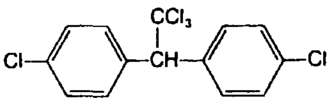
Compound	Molecular Weight	mp(°C)	bp(°C)	Solubility in H_2O ppm (temp, °C)[2]	Vapor Pressure	Partition Coefficient Octanol/H_2O
DDT	354.5	108.5		0.0034 (25)	1.9×10^{-7}(20)	1.55×10^{6}
Dieldrin	381	175-176		0.25 (25)	1.9×10^{-6}(20) 2.6×10^{-6}(20) 2.0×10^{-6}(20)	
1,2-dibromoethane (EDB)	187.872	9.97	131.65	3520 (20)	7.69 (20) 10.83 (25.1)	98.8
1,2-dichloroethane	98.960	-35.4	83.483	8450 (20)	62.1 (20.21)	25.0
2,4-D (acid)	221	140.5		522 (25)	0.4 (160)	6.4×10^{2}
Malathion	330	2.85		145 (20) 300 (30)	0.55×10^{-5} (20)	781
Parathion	291	6.1		11.9 (20) 11 (40)	3.78×10^{-5}(20) 1.96×10^{-5}(20) 4.39×10^{-6}(20) 5.7×10^{-6}(20)	6.4×10^{3}
Leptophos	412	70.2-70.6 71.5-72.0		.0047 (20) .03 (25)		2.0×10^{6}
Chlorpyrifos	350.5	42-43.5		.4 (23)	1.87×10^{-5}(25)	1.29×10^{5}
Phosalone	368	48		10 2.15 (20)		2.0×10^{4}
Carbaryl (Sevin)	201	142		114 (24)	< 0.005 (26)	
Propoxur (Baygon)	209	91.5		∿ 2000 (20)	3×10^{-6}(20)	
Chlorpropham (CIPC)	213.7	41.4	247	102.3 (25)		
EPTC (Eptam)	189		235	375 (25)	1.55×10^{-1}(25) 1.62×10^{-2}(23) 1.97×10^{-2}(24)	
Atrazine	215.7	173-175		33 ± 3.4 (25)	3.0×10^{-7}(20)	
Monuron	199	174-175		262 (25)	5×10^{-7}(25) 5.7×10^{-7}(25) 9×10^{-8}(27)	

of the halogenated hydrocarbons, one might expect that a high partition coefficient would be characteristic of the group. In contrast, the relatively good solubility in water of the alkyl phosphates such as dimethoate or malathion might lead one to characterize the OP's as having a low partition coefficient and hence, lacking propensity to bioaccumulate. This does not turn out to be the case, since some of the OP's such as dichlofenthion, leptophos have rather substantial partition coefficients and as a result readily partitions into fat.

With these caveats then, it is possible to give a general description of some of the more common classes of chemicals used as pesticides and cite specific examples of each class used as either an insecticide, herbicide, or fungicide.

Organohalogens:

DDT



1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane

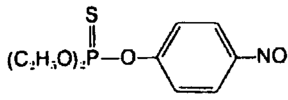
The organohalogens, that is compounds containing fluorine, chlorine, bromine or iodine, probably constitutes the largest groups of biologically active organic chemicals known. As indicated earlier, this is a broad class of compounds that can encompass hydrocarbons, organic acids, and many other chemicals. For the most part, however, this term or the more specific one - halogenated hydrocarbons - is used to designate chemicals containing carbon, hydrogen, and halogens.

One finds high biological activity in the halogenated methanes, e.g. chloroform and carbon tetrachloride, which are used as solvents or fumigants, as well as in polychlorinated aromatic compounds with melting points up to almost 200°C, and very low vapor pressures. It should be noted that the organohalogen compounds are not exclusively man-made chemicals. The carbonhalogen bond in aliphatic and aromatic compounds occurs extensively in nature. Not only are such compounds found in living organisms, as for example thyroxine, an iodine containing hormone, but it is believed that natural processes of the sea result in the formation of methyl iodide (40 million tons annually), and carbon tetrachloride (1.7 million tons annually). Even more complex organohalogen compounds have been identified from nature sources.

The organohalogens used as pesticides may include such simple compounds as carbon tetrachloride, or dicloropropene, ranging up to more complex chemicals such as DDT, dieldrin, phenoxy acids, and substituted ureas. As would be expected, there is a range of both biological and chemical properties among these different materials. It then becomes easier to classify some of the materials according to functional group rather than on the basis of their containing a halogen. Thus, we have the halogenated hydrocarbons represented by such things as carbon tetrachloride, dicloropropene, a soil fumigant, DDT, toxaphene and dieldrin. A substance such as Ronnel that contains three chlorine atoms is classified by the functional groups as a phosphorothionate derivative and hence is labeled an organophosphate.

Organophosphates:

ETHYL PARATHION



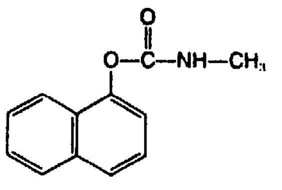
O,O-diethyl *O-p*-nitrophenyl phosphorothioate

These chemicals--for the most part insecticides although a few show activity as herbicides--are esters of one of the phosphorous acids. TEPP, for example, one of the first of the phosphate insecticides, is a simple ester of pyrophosphoric acid; while dichlorvos is an ester of orthophosphoric acid. The more widely used organophosphates are usually derivatives of thiophosphoric acid in which one of the oxygen atoms has been replaced by a sulfur atom. Malathion, on the other hand, is a dithiophosphate in which two oxygen atoms have been replaced by sulfur.

The phosphate esters, like any other ester, hydrolyze to yield phosphoric acid derivatives, and the corresponding phenol, or alcohol. In contrast to the chlorinated hydrocarbons, the organophosphates break down somewhat more readily, though some, such as parathion, are known to have considerable persistence under the proper conditions.

Carbamates:

CARBARYL (Sevin®)



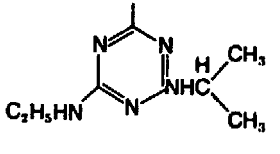
1-naphthyl methylcarbamate

The carbamates are derivatives of carbamic acid, a nitrogen-containing acid. The carbamate pesticides are usually esters except in the cases of a few dithiocarbamates which are sufficiently stable to be used as metal salts. The oxygen containing carbamate pesticides are esters in which either an aromatic or alkyl substitution has been made on the nitrogen atom. For the most part, those with the alkyl substitution on the nitrogen are insecticides and those with the aromatic substitution are herbicides, although in the case of aldicarb, the substituent on both the oxygen and the nitrogen are aliphatic.

Like the organophosphates, the carbamates hydrolyze readily and thus degrade fairly rapidly. The carbamates containing aromatic rings will have relatively low water solubilities (in the one to 100 ppm range), while the alkyl substituted carbamates will have solubilities more in the range of 100 to 200 ppm.

Heterocyclic Compounds:

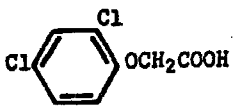
ATRAZINE



2-chloro-4-(ethylamino)-6-
(isopropylamino)-s-triazine

The heterocyclic compounds are materials containing rings made up of 4 to 6 atoms of which one or more atoms will be other than carbon. There may be more than one ring in the compounds, either in a condensed form or joined by a single bond. The atoms other than carbon going to make up the ring may consist of nitrogen (triazines, diazinon), sulfur (phosfolan), or oxygen (coumaphos). As might be expected from the divergent structures found in this group, the biological and chemical properties of the compounds vary widely. Some have high activity as insecticides, others herbicides and yet others as fungicides, rodenticides, etc.

Aromatic Acids:

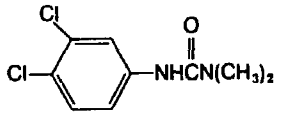


2,4-D

A number of aromatic acids and their derivatives are used as herbicides. Among them are the phenoxy acids and benzoic acids and their derivatives but very few have insecticidal properties. The aromatic portion of the molecule influences the biological and chemical properties of the compound, but the carboxylic acid portion determines in a large measure the physical behavior of the compound. Most are relatively strong acids that readily form salts and amides and can be esterified. Salts, for the most part, are water soluble, and the esters fat soluble. The volatility of the ester is markedly influenced by the molecular weight of the alcohol used to prepare the ester.

Ureas:

DIURON



3-(3,4-dichlorophenyl)-1,1-dimethylurea

For the most part, the ureas are considered to be herbicides, but recently the benzolphenyl ureas have been shown to be effective as larvicides. The ureas are derivatives of organically substituted urea, a common fertilizer. These compounds can have low water solubilities, and low mammalian toxicity.

There are a number of other organic classes represented among the various pesticides and growth regulators. Among them are included phenols, organometallic compounds, nitriles, quinones, and others. In addition to the insecticides derived from botanical origins such as pyreforum, derris and rotenone, there are, of course, also a number of compounds based on the chemistry of pyrethrum. Finally, there is developing a class of insecticides called the "biorational," exemplified by the various pathogenic insect viruses, such as polyhedrosis virus.

As is evident from Tables 2-1 and 2-2, there may be little relationship between classification by use and the actual chemical classes into which a pesticide may be placed. For that matter, even chemical classifications become somewhat arbitrary depending upon the detail to which the classification may be carried out. As an example,

Controlling Weeds with Chemicals

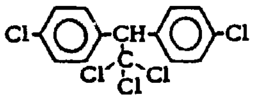
organic pesticides have been classified as to whether they are open-chain carbon compounds, cyclic compounds, or aromatic compounds; and then further classified according to the functions of these groups. Among the aromatic compounds these have been distinguished by whether they have rings composed entirely of carbon or whether they contain other elements (heterocyclic compounds).

Over the years there has developed an accepted chemical classification of pesticides, which includes such groupings as halogenated hydrocarbons, organophosphorus compounds, triazines, carbamate and organometallic compounds, etc. (Tables 2-1 and 2-2). (These are very broad categories, indeed, and even more refined classification schemes often have been used by pesticide chemists.) The physical and biological properties of members within the categories may be quite divergent; for example, among the compounds often classed as carbamates, one finds N-arylcarbamates used as herbicides, N-methylcarbamates as insecticides, the thiocarbamates as herbicides and the dithiocarbamates used as fungicides. Nonetheless, the broader groupings serve the useful purpose of categorizing chemicals roughly according to reactive parts of molecular structures upon which biological activity and environmental transformations are based, and, to some measure associating compounds of similar chemical and biological properties. The following Table (2-4) illustrates both category and structure of some commonly used pesticides.

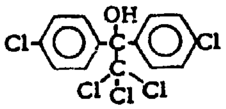
Table 2-4. A. INSECTICIDES

1. CHLORINATED HYDROCARBONS

a. Diphenyl Alkanes

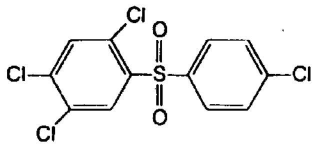


DDT



Kelthane®

b. Diphenyl Thioates

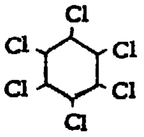


p-chlorophenyl 2,4,5-trichlorophenyl sulfone

Tetradifon (Tedion®)

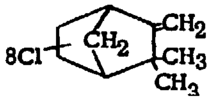
c. Polychloro Alicyclics

Monocyclic



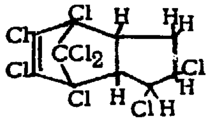
Lindane

Bicyclic



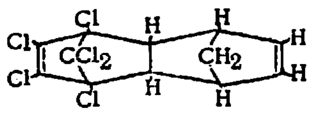
Toxaphene

Tricyclic



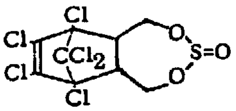
Chlordane

Tetracyclic



Aldrin

Hexacyclic

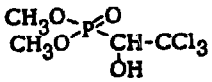


Thiodan®

Table 2-4. A. INSECTICIDES (continued)

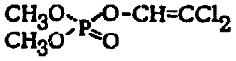
2. ORGANIC PHOSPHOROUS ESTERS

a. Phosphonate



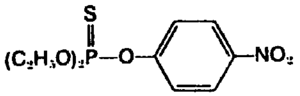
Dipterex®

Phosphate



DDVP

b. Thionophosphate

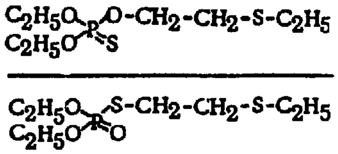


ETHYL PARATHION

O,O-diethyl *O-p*-nitrophenyl phosphorothioate

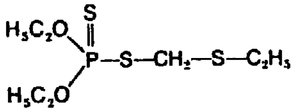
Parathion

Thiol phosphate



Systox®

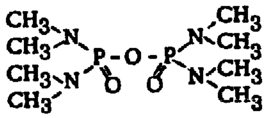
c. Dithiophosphate



O,O-diethyl *S*-(ethylthio)methyl phosphorodithioate

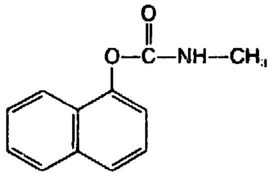
Phorate (Thimet®)

Amido phosphate



Schradan

3. CARBAMATES



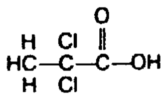
1-naphthyl methylcarbamate

Carbaryl (Sevin®)

B. HERBICIDES

1. CHLORO ORGANIC ACIDS

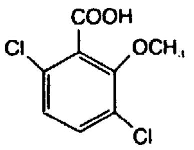
a. Chloro aliphatic acids



2,2,2-dichloropropionic acid

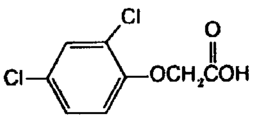
Dalapon

b. Chlorobenzoic acids



2-methoxy-3,6-dichlorobenzoic acid

Dicamba



(2,4-dichlorophenoxy)acetic acid

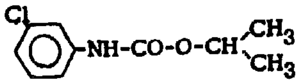
2,4-D

Table 2-4. B. HERBICIDES (continued)

2. NITROGEN COMPOUNDS

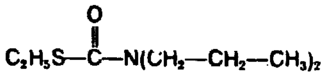
Mono-N Aliphatics

(Carbamates)



Dithio carbamate

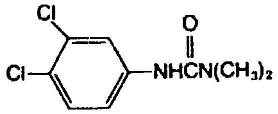
(Thio carbamates)



S-ethyl dipropylthiocarbamate

Amides

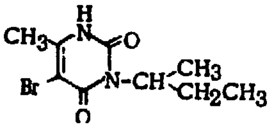
(Di-N alphatics)
Ureas



3-(3,4-dichlorophenyl)-1,1-dimethylurea

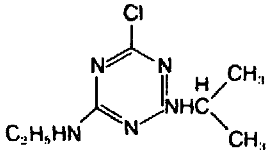
Diuron

(Di-N heterocyclics)
Uracils



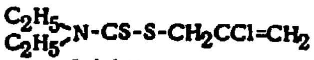
Bromacil

(Tri-N heterocyclics)
Triazines



2-chloro-4-(ethylamino)-6-(isopropylamino)-*s*-triazine

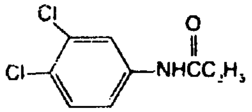
Atrazine



$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!>N\text{-}CS\text{-}S\text{-}CH_2CCl{=}CH_2$

Solubility in water 100 ppm.

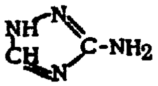
CDEC



3',4'-dichloropropionanilide

Propanil

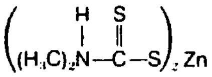
Triazoles



Aminotraizole

Table 2-4. C. FUNGICIDES

Dithio carbamates

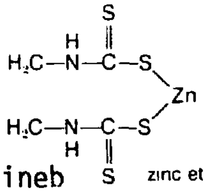


$\left((H_3C)_2\overset{H}{N}-\overset{S}{\overset{\|}{C}}-S\right)_2Zn$

zinc dimethyldithiocarbamate

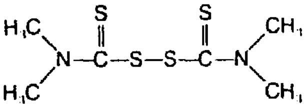
Ziram

Bis di thio carbamates



Zineb zinc ethylenebisdithiocarbamate

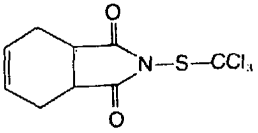
Thiurams



tetramethylthiuramdisulfide

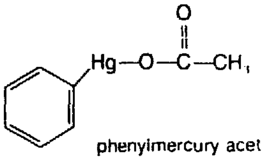
Thiram

Tetrahydro phthalimides



Captan N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide

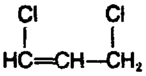
Organo mercurials



PMA phenylmercury acetate

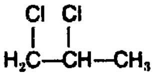
D. NEMATOCIDES

Halo alkanes



$\overset{Cl}{HC}=CH-\overset{Cl}{CH_2}$

and

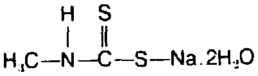


$H_2\overset{Cl}{C}-\overset{Cl}{CH}-CH_3$

1,3-dichloropropene and 1,2-dichloropropane

Dichloropropene-dichloropropane (D-D^{3})

Di thio carbamates



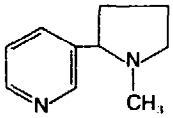
$H_3C-\overset{H}{N}-\overset{S}{\overset{\|}{C}}-S-Na.2H_2O$

sodium *N*-methyldithiocarbamate dihydrate

SMDC (Vapam®)

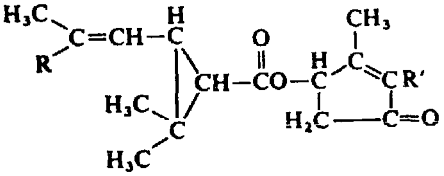
E. BOTANICALS

Generalized Structure: None
Natural



3-(1-methyl-2-pyrrolidyl) pyridine

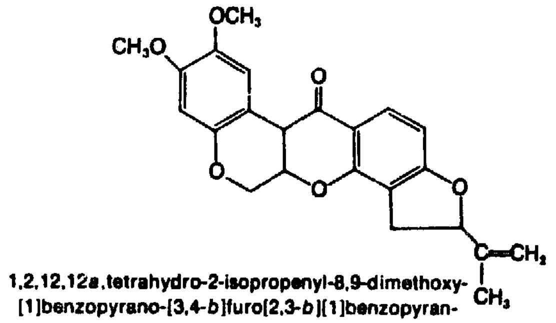
Nicotine



	R=	R'=
pyrethrin I	CH_3	$-CH_2CH=CHCH=CH_2$

Pyrethrum

Table 2-4. E. BOTANICALS (continued)



1,2,12,12a,tetrahydro-2-isopropenyl-8,9-dimethoxy-[1]benzopyrano-[3,4-*b*]furo[2,3-*b*][1]benzopyran-6(6a*H*)one

Rotenone

Ryania

$C_{25} H_{35} N O_9$

Sabadilla

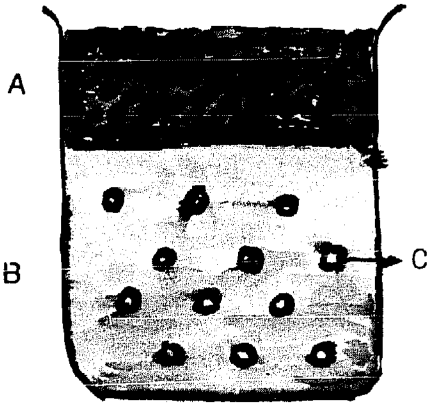
$C_{36} H_{51} O_{11} N$

PROPERTIES OF COMPOUNDS IN RELATION TO BIOLOGICAL ACTIVITY

The intrinsic toxicity of a chemical depends on (a) the atomic composition and molecular arrangement of the compound, and (b) the physical properties of the compound. In broad terms there is a commonality among living systems so far as their biochemistry is concerned. Thus, a compound that is an effective pesticide, for example a herbicide, if administered in a sufficiently high dose, will also effect a mammalian system. The difference in susceptibility between the plant and the animal is due to rather subtle differences in their biochemistry, and how the compound is distributed in the living body whether plant or animal.

Whether a given dosage of a chemical will be toxic to a particular organism depends in some measure on route of exposure. If there is an effective barrier, whether physical or chemical, the organism may be relatively unaffected. Thus, the human skin effectively reduces the entry of the ester form of 2,4,5-T into the human body, whereas the cuticle of the plant is a much less effective barrier, resulting in a high rate of absorption. Hence, the human is relatively unaffected by the small amounts of 2,4,5-T used in weed control, whereas, many broad leaf plants are destroyed by it. Similarly, there are organophosphate insecticides that are poorly absorbed by human skin, and others that are readily absorbed, as for example is the case with parathion.

One of the properties that has been found to be quite important in absorption of a compound and also in subsequent toxic action is the "partition coefficient." This is a term that describes the relative distribution of a compound between a lipid or fat-like layer and water when shaken in a two-layer system of the solvents. The most commonly reported partition coefficient is that between octanol and water. Octanol is chosen in part because of its similarity in properties to fats. Compounds with high octanol-water partition coefficients (accumulate in the octanol) are likely to bioaccumulate, i.e., deposit in fat at concentrations above the ingestion level. If, at the same time, the compound is refractory to breakdown by enzymatic, or purely - chemical means, it may persist in the body for a considerable period of time.



A - fat layer
B - water
C - chemical

Figure 2-1.

Figure 2-1 demonstrates the relationship between the partition coefficient and bioaccumulation by the accumulation of the chemical in the fat layer. This data clearly shows that the compounds having higher partition coefficients gain entry and accumulate in the organism. While many studies are based on bioaccumulation in fish, it has also been shown that when the partition coefficient lies within certain values, the compound will also penetrate human skin very readily. However, such penetration is a complex phenomenon, and does not relate exclusively to one physical property. Thus, some highly water-soluble compounds such as the alkyl substituted organophosphates, and carbamates penetrate very readily.

PROPERTIES VERSUS ENVIRONMENTAL BEHAVIOR (CHEMODYNAMICS)

Each chemical has a unique set of properties both chemical and biological that distinguish it from all other chemicals. This is illustrated by the table giving the properties of chemicals presented earlier in this chapter (Table 2-4). By measuring certain of these properties, for example, melting point, vapor pressure, water solubility, absorption of light or other electromagnetic waves, enables the chemist to uniquely identify the compound. However, these properties also are important in relation to how the chemical will behave when released in the environment. For example, a liquid with a high vapor pressure is immediately recognized as a volatile compound and one that will evaporate rapidly. An example of this is benzene or a more common mixture of chemicals, gasoline. In contrast, the high boiling liquids and solids, will have lower vapor pressures and thus be less volatile as is the case of lubricating oil.

It has been found that each chemical behaves a little bit differently in the environment and this difference in behavior is due to variation in the properties of chemicals and how they interact with the environment. Knowing the relationship between properties and behavior permits a prediction of how the chemical will behave in terms of sorption to soil and other solid material, rates of evaporation, water solubility and bioaccumulation. This field of study, termed "Chemodynamics," has become of increasing importance in recent years as we have sought to understand and be able to predict the behavior of chemicals in the environment. Very briefly, Chemodynamics assumes that: 1) the behavior, biological effects and persistence of the chemical results from the interaction of the chemical with components of the environment or the biota; 2) the type and extent of the interaction depends in part on the measurable properties of the chemical; 3) most of the non-metabolic interactions of the

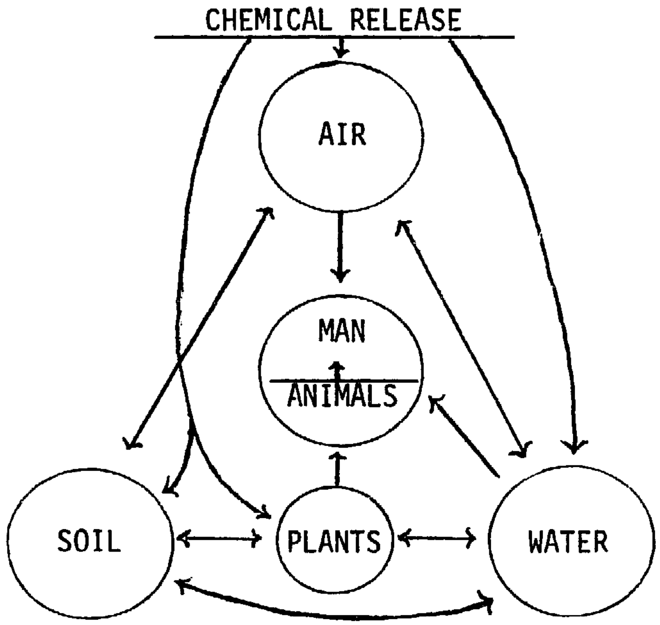


Figure 2-2. *Man's exposure to a chemical through cycling of residues in the environment.*

chemical are to varying degrees reversible; and 4) knowing something of the nature of the interaction in relation to the property of the chemical. Having the measured property of the chemical--a first approximation prediction of the behavior and biological effect of the chemical can be made.

Energy (sunshine) flux as well as wind and water movement are the driving forces for movement of chemicals. Moisture, nutrient level and temperature as well as light intensity influence the degradation in the environment e.g., soil, air, water. The complexities of movement or transport is illustrated in a simplified way in Figure 2-2.

When a chemical is released in the environment, e.g. spraying of pesticide, it may be thought of as going through four steps in exerting its biological effects. First, of course, is interaction with the environment; the next is transport to and interaction with the boundary of the organism; third is movement through the organism with all the complex interactions; and finally the interaction at the active or sensitive site. In all of these steps a number of physical chemical processes are operative. The processes operative at each of the steps is illustrated in the following table.

Table 2-5. Processes Involved in Chemical Action

Steps	Processes
Interaction with the environment.	Adsorption of surfaces Vaporization Photochemical breakdown Autochemical breakdown Dissolution Partitioning various reactions
Interaction with barrier of organisms.	Adsorption Destructive reactions Rejection
Intracellular transport.	Adsorption Metabolic binding Metabolism Partitioning
Reaction with critical site.	Adsorption Reaction

From the foregoing it can be seen that there are some general processes or reactions common to two or more of the steps.

Adsorption:

As indicated, the behavior of chemicals in the environment is strongly influenced by the physical properties of the chemical. The properties influence the degree to which the chemical will be sorbed (bound up) by soil, organic matter and clay, and subsequently the leaching with water and the rate of vaporization.

Repeated studies have shown that the bulk of the pesticide applied to crops ultimately finds its way to the soil. There it is bound (sorbed) reversibly by the various soil components through either physical or chemical forces. The principal soil constituent for sorbing pesticides is the organic matter though the clay fraction of the soil is also important. For many pesticides, the interaction or adsorption is governed by their physical properties. For example, the lower the solubility of a pesticide in water, the more its tendency to adsorb on soil particles. One must distinguish between the extent to which a chemical is adsorbed and the strength with which it is bound. The strength of this binding is related both to the properties of the soil and significantly to the latent heat of solution (in water) of the pesticide.

Adsorption of pesticide on clothing

Adsorption on soil (Haque and Freed, 1975) or any other surface can be taken as analogous to fruit or coffee stain on a piece of cloth. Here the colored material from the fruit or coffee is sorbed by the cloth. Depending on the nature of the textile as well as the nature of the material that caused the stain, the spot may be difficult, or easy to remove.

As mentioned above, the adsorption is a reversible process. That is, there is always the possibility for a certain amount of the chemical to be released from the sorbed state. Hence, it is found that with a given concentration of the pesticide, a certain fraction will be found sorbed on the soil particles and the remainder will be found in solution or as the vapor.

If the amount of the chemical in the free state is reduced by leaching or escapes as a vapor, more of the bound materials will be released. Thus, an equilibrium of sorts is established between the surface of the soil particle and the concentration of the chemical immediately surrounding it. If a chemical is strongly bound by the soil constituent, more energy is required for its release; hence, most of the chemical will be sorbed with only small amounts found in the free state. The only exception to this is when excess quantities of chemicals are used in which case the sorbing surface is saturated before appreciable quantities of the chemical are used up.

The rate and extent of the processes are related to the physical and chemical properties of the compound. For example, the water solubility and/or octanol/water partition coefficient indicates the tendency of the compound to sorb on different surfaces as well as movement across the boundary of organisms for accumulation. Similarly the vapor pressure is an indicator of the readiness of volatilization and hence, the rate at which the chemical will evaporate from a surface. Table 2-6 indicates the physical chemical characteristics and their relationship to such fundamental behavior in the environment as adsorption, leaching, vaporization and breakdown.

Table 2-6. Relation of Physico-Chemical Properties to Environmental Behavior

Physical Chemical Data	Related To
1. Solubility in Water	Leaching, degree of adsorption, mobility in environment
2. Partition Coefficient	Bioaccumulation potential, adsorption by organic matter
3. Hydrolysis	Persistence in environment or biota
4. Ionization	Route and mechanism of adsorption or uptake, persistence, interaction with other molecular species
5. Vapor Pressure	Atmospheric mobility, rate of vaporization
6. Reactivity	Metabolism, microbiological, photochemical and autochemical degradation

Of the various processes in the environment, those particularly related to overall environmental behavior include; sorption, leaching, vaporization, degradation and in terms of biological effect, bioaccumulation. Each of these processes will be treated individually, but it must be remembered that there is an interrelationship among them. For example, if one is concerned with the uptake and accumulation of a chemical by an organism it must be remembered that adsorption on a particle of soil or sediment will substantially reduce the amount of chemical available for uptake. Thus, if the accumulation is by a fish, the same concentration of chemical in water free of sediment will result in a greater uptake than if there is a heavy silt load in water.

Sorption regulates or influences further behavior of the chemical in the soil. For example, if a chemical is strongly bound by soil, less of it is available for biological activity (Green, et al., 1977; Haque & Freed, 1975). It is not uncommon to find that in certain highly adsorptive soils, the biological activity of such chemicals as chlorinated hydrocarbons, the urea herbicides or triazine herbicides will be substantially reduced by adsorption. Thus, it has been observed that toxicity of chemicals may be reduced in soil or by particulate matter in water.

Similarly, leaching or movement of the chemical with water is influenced by the extent and strength of sorption (Ind. Prod. & Formul. Pest. in Dev. Countries, 1972). The tendency of chemicals in soil is to move in the direction that water is flowing. Hence, if rain is falling on the surface of the soil and water is moving down through the soil profile, the water will tend to carry the chemical downward. On the other hand, if vaporization is occurring from the surface and the bulk of the water movement is toward the soil surface, this will tend to carry the chemicals in the soil upward. The deposits of salts on surfaces of soils in certain arid regions are an illustration of this. The chemicals that are poorly adsorbed by soil move quite freely with the water. Thus, a substance like the nitrate ion or certain organic acids will move readily in soil. On the other hand, the strongly bound materials, such as the chlorinated aromatic hydrocarbons or the triazine herbicides will scarcely move at all. Indeed, it has been reported that even after many months such chemicals will not move out of the surface two or three inches of soil.

Sorption also modifies the tendency of volatile substances to escape from the soil as vapors. The binding reduces the vapor pressure or volatility well below that of the chemical in its normal state.

Sorption, likewise, influences the degradation of chemicals in soil. Any organic chemical, when introduced into the soil, is subject to degradation forces. Degradation of the chemicals in soil may come about by either biological degradation or chemical degradation. Because of the wide variety of species of organisms in soil, there is usually at least one that is capable of attacking almost any type of organic structure. As a result, the chemical is degraded to other products and ultimately the elements. With more reactive chemicals, the process may be very rapid and with others slow. Moreover, as noted earlier, temperature, moisture, the texture of the soil and many other environmental factors influence this process. However, the sorption may determine the availability of the chemical to the organisms and, hence, will materially affect this rate at which the biological degradation will occur.

Chemical degradation, on the other hand, may actually be favored by sorption, particularly if it is a catalytic or surface type of chemical degradation. In this instance, the tendency to be bound by the reactive surface will foster the reaction. On the other hand, if the reaction occurs in solution, as for example in the case of hydrolysis, the adsorption would substantially alter the reaction rate.

It has been found in a number of studies that a quantitative relationship can be determined for a given amount of soil and a given amount of chemical. This is very similar to what is found in study of adsorption in physical chemistry. The most commonly used relationship is the so-called Freundlich relationship. This relationship is determined by measuring the amount of chemical adsorbed using several different concentrations of the chemical as a starting solution. The relation then, is expressed as:

$$\frac{X}{M} = K\,C^{\frac{1}{N}}$$

Where X over M is the amount of the chemical adsorbed per gram of soil, K is a constant, C is the equilibrium concentration after adsorption, and $\frac{1}{N}$ is a constant.

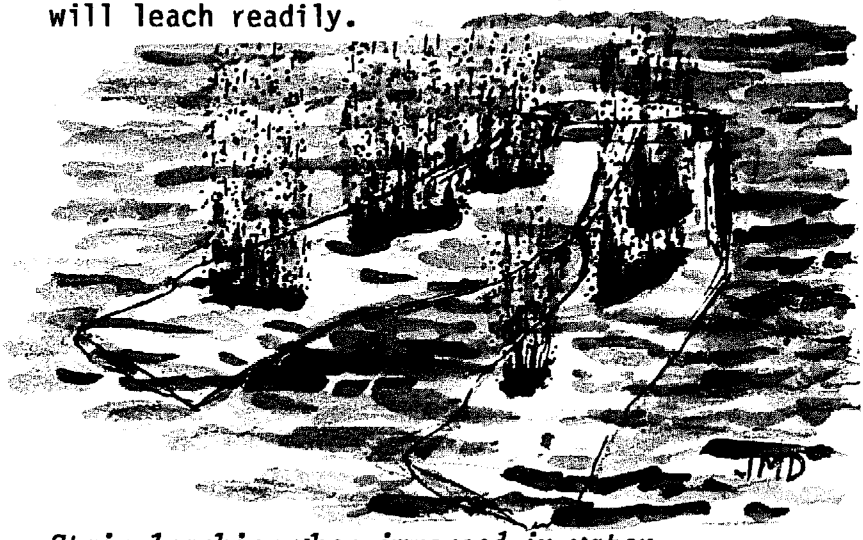
Leaching:

Leaching is the term that is applied by movement of a chemical through soil with the flow of water. The movement is usually downward and laterally though at times when the evaporation from the soil surface is great, the bulk flow of water may be upward.

Leaching, of course, is much more of a problem with a pesticide that is applied to the soil than one applied to a standing crop. Nonetheless, because so much of the chemical does reach the soil, regardless of the purpose of application, the movement through the soil must be considered. If the chemical is carried into the soil, it may remain there as a residue that can contaminate a subsequent crop, or if it is a highly mobile chemical it may be leached into the ground water and ultimately reach streams.

Soil type and the percent organic matter as they influence adsorption and water penetration rate, as well as the properties of the chemicals are all important in leaching. In a given soil type, the properties of the chemical are very important in relation to leaching, since these properties determine how tightly the chemical may be adsorbed. For example, the chlorinated hydrocarbon insecticides such as DDT, aldrin, dieldrin and heptachlor, by virtue of their low solubility in water and strong adsorption, are leached but very little. Some of the organic phosphates such as parathion are leached somewhat better than the chlorinated hydrocarbons but even they are not highly mobile. On the other hand, there are certain types of pesticide that are only poorly adsorbed by soil and are quite water soluble which move very freely in the soil. This is particularly true of certain of the herbicides. In leaching, the chemical moves with the water flow, thus if the water is percolating downward so does the chemical. However, if the water movement is upward as in evaporation from the surface, some of the chemical will move upward resulting in spreading the chemical through the soil profile.

It will be remembered under "Adsorption," that we compared sorption to the staining of a piece of cloth by fruit or coffee spills. Leaching may be compared to removal of that spot by washing. If the stain is quite persistent, it would represent a chemical such as one of the chlorinated hydrocarbons that are resistant to leaching because of the strong adsorption. On the other hand, if it is readily removed, it is more like a substance that will leach readily.



Stain leaching when immersed in water

Another analogy might be where there is a stain in the cloth and a little water is applied to the spot with the resulting spread of the spot with an obvious dilution as indicated by a less intense color. In this case the colored material has moved or "leached" with the water.

A number of attempts have been made to model leaching in relation to soil type, chemical properties, and amount of water percolating through the soil. The complexity of this problem makes it difficult to get a simple mathematical expression of these relationships. However, one empirical expression has been found to be quite useful.

$$C_X = \frac{Q}{\sigma\sqrt{2\Pi}} e^{-\frac{(X-X_0)}{(2\sigma^2)}}$$

Where C_X is the concentration at depth X, Q is the amount applied, and sigma is the spreading coefficient. As will be recognized, this equation is based on chromatographic theory.

Vaporization:

At normal temperatures most organic chemicals have a tendency to change into a vapor. This is a result of the chemical receiving energy from its environment which increases the kinetic motion of the molecules of the chemical giving them a tendency to separate from the surrounding molecules and escape into the atmosphere. The chemist measures this tendency as vapor pressure. The pesticide chemicals may have an appreciable vapor pressure as is the case with ethylene dibromide, a fumigant, through compounds of intermediate vapor pressure such as carbamates or organic phosphates, to quite low vapor pressure such as certain of the chlorinated aromatic hydrocarbons, to extremely low vapor pressure such as the alkali salts of organic acids.

The vapor pressure of a compound is one of the characteristic properties at a given temperature. As temperature increases, the vapor pressure also increases resulting in a more rapid evaporation as illustrated by boiling water. Vapor pressure can be measured by appropriate techniques in the laboratory, but this does not tell us at what rate the compound will vaporize. It is, however, possible to approximate the rate of vaporization by the following equation:

$$Q = \beta P \sqrt{\frac{M}{2\Pi RT}}$$

Where Q equals the grams vaporizing per square centimeter per second; β is approximately 2 X 10^{-5} ,βM is the molecular weight, R is the gas constant and T is the temperature in degrees absolute. While this equation was developed for rates of evaporation from the chemical's own surface, under still air, it does give us a means of estimating rate of evaporation from other surfaces. However, if the compound has been adsorbed by or mixed with soil, the rate of evaporation will be reduced to 10% or less of the calculated rate (Haque & Freed, 1975). This is in part due to the compound being held by the forces of adsorption and in part to restriction of vapor escape by the soil.

Environmental factors that influence rate of evaporation include wind velocity, temperature, moisture, and the type of adsorbing surface. Generally, as wind velocity and/or temperature increases, the rate of vaporization will also increase.

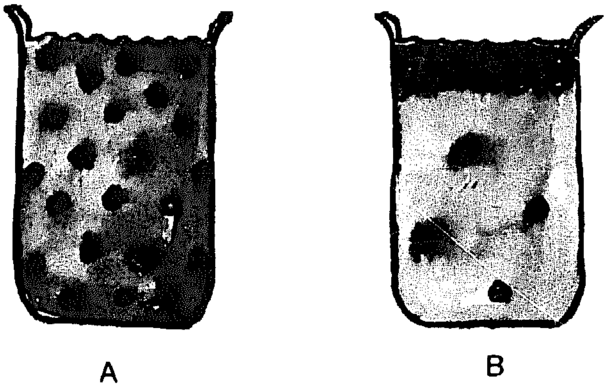
A form of vaporization

It is obvious that the larger the surface area of chemical exposed the more chemical will evaporate in a given time. Hence when the chemical is spread out over a large land area, the chemical has a greater opportunity for vaporization. However, the adsorption of the chemical by the soil particles, discussed earlier, reduces this vaporization several fold. If this were not the case, practically any chemical applied to the soil surface would be lost so rapidly as to be ineffective. Nonetheless, measurable quantities of chemicals may volatilize from the soil surface. Chemicals with a relatively high vapor pressure that are poorly adsorbed will be lost in greater quantities. On the other hand, though a chemical may have a measurable vapor pressure, if it is strongly bound, its rate of loss will be lower. It has been demonstrated in a number of instances with a variety of chemicals that vapor loss does occur, sometimes in quantities sufficient to cause contamination of air and adjacent areas.

It has been frequently observed that there is usually more chemical loss from a moist soil than a dry one. This has been ascribed to a phenomenon called codistillation. It has been pointed out by several authors, however, this increased loss from moist soil during vaporization of water is probably due to the water displacing the chemical adsorbed on the soil particle rather than any particular effect of the water vapor loss on the rate of volatilization of the pesticide (Green, et al., 1977; Haque & Freed, 1975).

Solution Behavior:

As has been pointed out, practically all of the known pesticides have a measurable solubility in water. The solubility may be very low being a few tenths of a part per billion in the case of some compounds and ranging up to quite high water solubilities in the case of others. The solubility in part depends upon the polarity or electrical properties of the compound as well as its intrinsic elemental makeup. The solubility and behavior of compounds in water is of considerable importance in considering the environmental impact of chemicals.



A - water soluble chemical
B - chemical poorly soluble in water
Figure 2-3.

If the pesticide in question is an ionizable one, such as an acid, base or salt of either of these, the solubility is likely to be greater than that of the less polar materials such as the chlorinated hydrocarbons, organophosphorous compounds or the carbamates. Of these latter, less polar compounds, tend to gather at surfaces in water which may be either at the air-water interface or at the surface of colloidal particles in water. Where the surface or interface is with another liquid immiscible with water such as a fatty solvent, the tendency of the chemical to escape into this solvent from water is called partitioning.

Where the compound is one of the less soluble and less polar chemicals, the sorption onto the suspended matter in water or partitioning into oil layers on the water surface tends to take the chemical out of the bulk of the water. With many substances it is found that filtering the suspended matter from the water removes the greater part of the pesticide from the water. It is probable, therefore, that much of the pesticide carried by water is in fact carried by particulate matter suspended in water. Further confirmation of this comes from studies of transport of chemical in flowing streams. Here it has been noted that there is "chromatographing" tendency of the material that is felt to be due to the solid material alternately being deposited on the bottom of the stream and picked up again in the turbulent motion of the water. Ultimately, the pesticide carrying particles do settle out and remain on the bottom.

It may be noted in passing that as a salt concentration of water increases, the solubility of most compounds tends to decrease.

Pesticide Spill by Stream

Leakage of Pesticides into Stream

Uptake and Accumulation:

The accumulation of pesticides by organisms is frequently observed. This accumulation results in residues that may be of concern. The mechanism by which materials are accumulated is complex and varied. Many compounds are accumulated through the metabolic activity of the organism, direct ingestion, or it may be through a physical mechanism or all of the processes. With many of the compounds used as pesticides, the uptake can be related to a physico-chemical property called the partition coefficient. If the partition coefficient is high, the compound will accumulate in organisms of the food chain with successive increases at each step. This is illustrated by the accumulation of a pesticide by fish in the accompanying drawings. This partition coefficient is a measure of the distribution of the chemical between a lipophilic and a hydrophilic or aqueous state. The following equation is the simplest form indicating this relationship.

$$K = \frac{C_O}{C_{H_2O}}$$

The partition coefficient is characteristic for the compound and is dependent on a variety of molecular features of the chemical. However, many studies have demonstrated the value of the partition coefficient in estimating the ease with which a chemical, particularly a non-polar or non-ionized chemical, will be accumulated by a living organism exposed to it.

Partition coefficient is also a good index of the possible adsorption of a compound by soil organic matter. This together with molar refraction and/or latent heat of solution all give an indication of the adsorbability of compounds.

Degradation:

One of the important considerations of fate and behavior of a chemical in the environment and its effectiveness as a pesticide is the manner and rate at which it breaks down. All organic pesticides, when introduced into the environment, are subjected to physical and biological forces. The action of these forces results in breakdown of the chemical. This explains why wood rots, metals corrode and rust, or plastics break down.

For some compounds the breakdown or degradation is principally biological; that is, the compound is destroyed by metabolism of plants and microorganisms. The degradation of the compound is brought about by the action of the various enzymes secreted by the organisms. Other compounds are susceptible to ordinary chemical attacks, such as hydrolysis, or they may be subject to photochemical breakdown (Green, et al., 1977; Haque & Freed, 1975; Sheets & Pimentel, 1979).

Practically all chemicals will absorb light of one wavelength or another depending on the nature of the chemical. At an appropriate wavelength of light, the energy is great enough to result in modification or breakdown of the compound. This illustrated by the following.

$$\text{Chemical} + \text{light} \longrightarrow \text{breakdown products}$$

Even though the shorter wavelengths at the ultraviolet range are absorbed by the ozone layer, the wavelength of sunlight reaching the earth's surface, particularly at higher altitudes and in the tropics, will be sufficient to bring about a reaction in most compounds. If in addition, there is present hydrogen donors such as certain oils or water, the rate of photochemical decomposition increases. Moreover, if the compound is particularly unstable, the wavelengths may be sufficient to produce free radicals that lead on to decomposition.

Adsorption on surfaces may either increase or decrease the rate of photochemical decomposition. The decomposition can occur in solution and most probably does occur in the gaseous state. Photochemical decomposition is probably one of the reasons for the relatively short residual life of many chemicals.

Ordinary chemical reactions such as oxidation, reduction and hydrolysis can also occur in the environment. With many chemicals, there is no need for biological intervention for these reactions to occur. Many organophosphates, for example, are readily hydrolyzed at the pH's commonly found in soil. This is illustrated by the following reaction:

$$\text{parathion} + \text{water} \longrightarrow \text{paranitrophenol} + \text{alkyl phosphate}$$

Adsorption on clays or organic matter increases the rate of breakdown of some chemicals by fostering either hydrolysis or some other chemical reaction.

The biological reactions resulting in degradation of chemicals cover the range of oxidation, reduction, hydrolysis, dealkylation and so on. These reactions are mediated by the different enzymes secreted by the organisms or free enzymes in the medium.

Of concern to us is the rate at which the chemical is degraded (Green, et al., 1977; Sheets & Pimentel, 1979). This influences the length of time the chemical persists to give control of the pest or result in undesired residues. Rates of decomposition of various pesticides has been most extensively studied in soils. In many instances, the soil decomposition appears to follow a pseudo-first order kinetics as illustrated in the following equation:

$$C_x = C_o e^{-kt}$$

C_x = concentration at time, x; C_o = initial concentration; t = time;

k = reaction constant; and, e = base of natural logarithms.

However, a more generalized equation has been proposed, called the "power rate model," as illustrated in the following equation:

$$C_x = KC^n$$

C_x = concentration at time, x; K = reaction constant; and, n = "power" constant.

The rate of decomposition in the soil has been found to be influenced by moisture, temperature, soil type, absorption and of course, the level of nutrients and biological activity. Temperature has proven to be an important factor up to the temperature critical for the activity of organisms. If one were desirous of estimating the length of time a chemical persists at a given temperature knowing its rate or ite energy of activation, persistence at another temperature may be estimated by applying the Arhennius equation:

$$\log \frac{K_2}{K_1} \times \frac{\Delta h}{2.3 R} \times \frac{\Delta T}{T_2 \times T_1}$$

K_1, K_2 = reaction constants at temperatures T_1, T_2 (Kelvin); Δh = enthalpy of reaction; R = molar constant, 1.987 cal mole^{-12}; and, $\Delta T = T_2 - T_1$.

Many of the pesticides studied have been shown to breakdown at a rate that can be described by the first-order rate law. This has given rise to the terminology of half-life based on the so-called half-life calculated from the first-order kinetic equation. Actually what is being described in this instance is the time required for one half of the chemical to disappear. While not completely accurate, it is nonetheless a useful concept and a reasonable way of comparing the persistence of one chemical to that of another.

Not infrequently the layman, in expressing concern about pesticides or chemicals in general, speaks of the continuing accumulation of these products in soil. There is an apparent misconception that many of these chemicals undergo no degradation and continue to accumulate in subsequent applications. This obviously is not the case since the chemicals do undergo a degradation, and even with successive applications the concentration will decline. To illustrate this point let us take a chemical having a 12-month half-life that is applied in annual applications at the rate of 2 lbs/acre. Figure 2-4 then illustrates what we can readily calculate; namely that the maximum concentration that will ever be achieved is twice the annual application of 2 lbs/acre or approximately 2 kg/hectare.

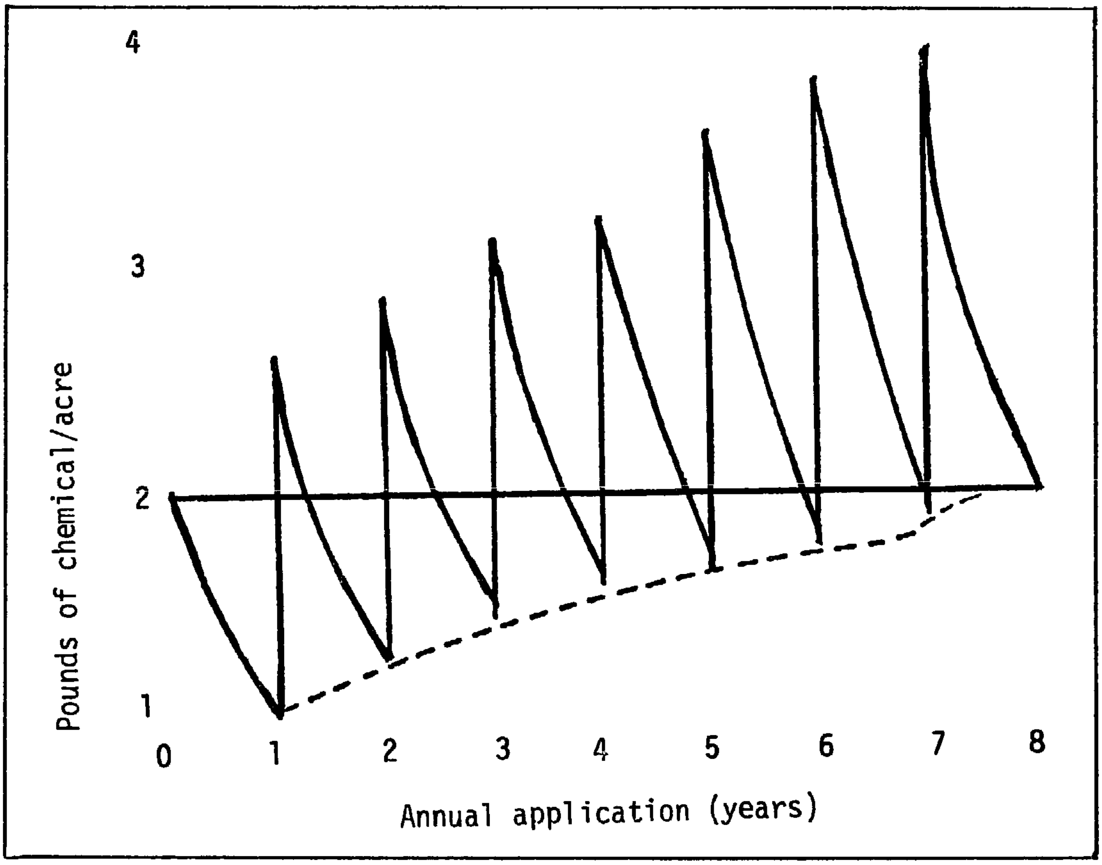


Figure 2-4. *Trends in Soil Residue Level With 2 Pound Annual Application of Chemical with 12 Month Half-life*

CONCLUSIONS

What has been presented is some information on how the properties and chemistry of a pesticide relate to the different processes in nature and how this influences the transport, persistence, activity and ultimate fate of the chemical. Through this understanding, we gain an appreciation of how the vapor pressure relates to movement by wind, solubility and adsorption to movement by water, and the oil solubility to uptake by living organisms. Similarly, we gain an insight on the probable persistence of the compound by knowing some of the reactions that it undergoes.

When we are able to predict the probable behavior of the pesticides from its properties, we are then in a position to use that information for safer and more effective application of the chemical. For example, if the vapor pressure indicates that the material is likely to evaporate very rapidly, we can modify the formulation and method of application to reduce the loss of the chemical by this route. By so doing, the chemical can be more effective and less of it used. Obviously, to be able to use less chemical and still obtain the degree of control is going to be less expensive.

This same information and understanding about the chemical will permit its use in a manner that is much safer to both man and the environment. Equally important, is that such information will enable us to use the chemical in a more rational manner in integrated pest management. Thus, the basic information will lead to the formulation and application of the chemical in such a way as to protect beneficial organisms and allow the successful use of other husbandry practices.

At first glance it would appear that there are many complexities regarding the relationship of chemical properties to the behavior of a pesticide in the environment. However, it now appears that there are three major facts that one needs to know about a chemical in order to use it in the safest and most cost effective manner. These three facts are:

1. water solubility,
2. vapor pressure, and
3. susceptibility to different reactions.

As has been shown in this chapter, water solubility is related to the partition coefficient which in turn is an indication of the adsorption of the chemical as well as biological accumulation. The vapor pressure is an excellent indicator of the amount of material that will volatilize during and following application. The susceptibility to reactions whether photochemical or biological, will indicate the probable persistence of the chemical and hence the length at which it will give control.

These three properties of the chemical can be determined at least in a qualitative fashion with the simplest of equipment. It can be done in the laboratory, thus avoiding long and expensive field studies. Vapor pressure for example, can be obtained to a reasonable approximation by simply weighing the amount of chemical lost from a given area and then calculating the vapor pressure. The determination of water solubility is a little more difficult, but can be done in a crude fashion by addition of small amounts of the chemical to a given volume of water and observing the rate at which it dissolves. Better of course is a direct determination of the chemical in a saturated solution by an appropriate analytical technique. The analytical technique, however, can be so simple as a biological assay.

The foregoing information has a direct application in the formulation, use, and disposal of chemicals. Applying this knowledge to the problems encountered in handling, transport, and use, as well as disposal, can avoid many problems.

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Chapter 3

Epidemiology of Pesticides

Davies, J.E.

SUMMARY

Since pesticide exposures are ubiquitous, their possible adverse health constitute a serious agromedical problem. The development of both acute and chronic illness as a result of pesticide exposure are health issues which are of serious for agriculture and health. This Chapter, in reviewing some of the literature on cancer epidemiology and pesticides describes the health effects which have been related to chronic exposure and reviews the research potential of different epidemiologic types of studies.

INTRODUCTION

There are many definitions of epidemiology but one which has widespread acceptance is that of MacMahon and Pugh (1970), which states that "Epidemiology is the study of the distribution and determinants of disease frequency in man."

Insofar as pesticides are concerned such a definition requires that we must fully understand the subtle variables which influence human exposure to pesticides. Human pesticide exposure is not straightforward and laboratory studies show that the person whom we suspect is only mildly exposed, is often ultimately found to have significant exposure. These subtle differences of pesticide exposure are discussed in some further detail in the chapter on Human Pesticide Exposure Assessment.

Pesticides can be toxic to all forms of life and man is no exception. They are ubiquitous, many are acutely toxic, some are persistent, some can biomagnify, some are carcinogenic, others mutagenic and teratogenic. Understandably therefore the public is vitally interested in finding out whether the types of human exposures that are presently sustained as a result of modern pesticide management practices, are harmful in any way.

The objective of all epidemiological studies is to demonstrate an association between exposure and outcome, and the discipline offers a direct and concise approach to the study of those diseases which are related to pesticide exposure. All three types of epidemiological studies, descriptive, experimental and analytical have clarified the various risk factors associated with different pesticide exposures.

Categories of Pesticide Exposure

From an epidemiologic point of view, there are three types of pesticide exposures. These are: acute, chronic occupational, and incidental, and are shown in Figure 3-1. together with some of the associated adverse health effects.

Acute exposure results in systemic poisonings and topical effects on various tissues of the body, particularly on the skin and in the eyes. Descriptive epidemiologic studies have demonstrated who is at special risk and these findings are discussed in Chapter 5, Pesticide Poisonings - Who Gets Poisoned and Why?

Incidental pesticide exposure is concerned with the distribution and determinants of the trace amounts of pesticide residues in our ambient environment and those which are stored in adipose tissue. These are discussed in more detail in Chapter 11, which is entitled Pesticide Monitoring and Human Concerns. Descriptive epidemiologic studies on pesticide have helped delineate the demographic and geographic variabilities of the DDT residues in different population groups. Studies have shown the importance of house dust in tropical climates and brought out the point that these sources are just as important contributors to the DDT body burden in tropical climates as is food (Davies, et al., 1975).

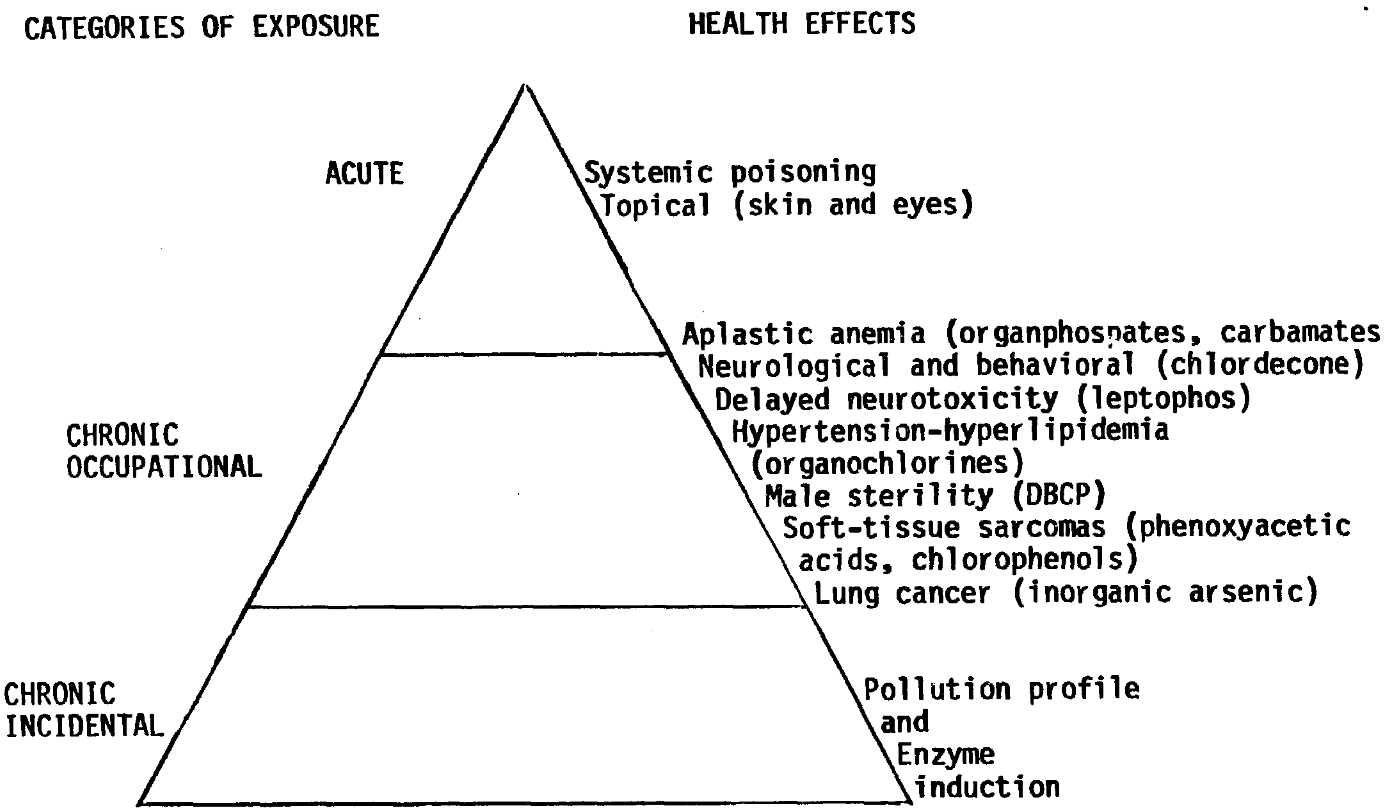

Figure 3-1.

Recent studies on DDT residues in people living in Triana, Alabama showed that high values of DDT were linked to the eating of fish contaminated with this pesticide. The source of the pesticide was ultimately traced back to the discharge of DDT from an upstream manufacturing plant into the river; serum Total DDT values in 492 residents, 85% of whom were black, ranged from 0.6 to 2,820 ppb with a geometric mean of 76.2 ppb (Kreiss et al., 1980).

Since acute poisonings and incidental exposures are discussed elsewhere, this chapter on Pesticide Epidemiology will concentrate on the middle area of Figure 3-1 and will discuss some of the disease entities which have been related to chronic occupational pesticide exposure, especially the carcinogenicity risk of occupational pesticide exposure.

Analytical studies

A variety of different types of epidemiologic studies have looked into the association of chronic disease with occupational pesticide exposure. Morgan (1980) summarized some of these effects in Table 3-1.

Table 3-1. Adverse Effects of Pesticides

Chronic Effects (delayed onset, or protracted, recurrent, or irreversible course)

A. Peripheral neuropathy
B. Effects on reproduction
C. Sensitization
D. Suspected, but generally unconfirmed effects
   - ? effects on brain, heart, liver, kidney, lung, blood, reproductive organs
   - ? accelerated atherosclerosis, hypertension
   - ? carcinogenesis
   - ? teratogenesis
   - ? impaired immunity and immunopathies

Adapted from: Morgan, D.P., 1980

Within the last 10 years, several epidemiological studies, most of them case-control but including a few retrospective cohort studies, have described associations of occupational pesticide exposure with a variety of chronic diseases. These diseases, some of which may persist from a few months to years, have been recognized in a variety of different organs, and no organ appears to be exempt.

In the reproductive area, the association of occupational exposures to dibromochloropropane (DBCP) with impaired male fertility was an important observation (Whorton, et al., 1977). This was first recognized when a number of cases of infertility were discovered among men in a California pesticide formulating plant. The suspected cause was exposure to 1,2-dibromo-3-chloropropane. The major effects, seen in 14 of 25 nonvasectomised men, were azoospermia or oligospermia and raised serum levels of follicle-stimulating hormone and luteinizing hormone levels.

The duration of chemical exposure to dibromochloropropane was significantly related to these abnormal findings and workers with sperm counts of <1 million had been exposed for at least three years. None with sperm counts above 40 million had been exposed for more than three months. Differences in testicular function would not have been expected to have resulted from the small age differences noted in the two study groups (Table 3-2).

Table 3-2. Comparison of DBCP Exposure in 11 Workers With Low Non-vasectomised and Normal Sperm Counts

Sperm-count (x10 ^{6}/ml)	Group	Age (yr)	Exposure (yr)	F.S.H. (mI.U./ml)	L.H. (mI.U./ml)	Testosterone (ng/dl)
0.2+0.1*	A	32.7±1.6**	8.0±1.2**	11.3±1.8***	28.4±3.3****	459±35
93+18	B	26.7±1.2**	.08±.02**	2.6±0.4***	14.0±2.8****	463±31

* All results given as mean + standard error of mean
** Difference between groups A and B significant at the P <0.01.
*** Differences between groups A and B significant at the P<0.001.
**** 9 workers with 0 sperm/ml, 2 with 1 x 10^6/ml.
Modified from: Whorton, D. et al., 1977.

Male reproductive disorders manifested by sterility, oligospermia and sperm hypomotility were also noted in Hopewell, Virginia in a small factory manufacturing Kepone® (chlordecone). Symptoms found in these workers whose exposure to Kepone® was excessive demonstrated involvement of other systems besides the reproductive system. Thus, evidence of involvement of the central nervous system was indicated by the following central nervous system manifestations: tremors, stuttering speech, opsoclonus, and pseudomotor cerebri (Cohn, et al., 1978). Serious derangement of the central nervous system was also suggested among workers manufacturing leptophos (Phosvel®). In a health study of workers manufacturing leptophos and conducted by the National Institutes of Occupational Safety and Health, investigators found that an unusual number of workers had neurologic abnormalities, electromyographic and psychological performance abnormalities (AOMA Report, January, 1978). Delayed neurotoxicity can occur with this pesticide, and this was first seen in Egypt when leptophos was incriminated in the accidental death of 1,300 water buffalo as the major neurologic manifestation of this insecticide (Near East News Roundup, 1971). This has been reproduced experimentally in hens by Abou-Donia and Pressig, 1976.

In the cardiovascular area, hypertension and hyperlipoproteinemia were observed more frequently in occupationally exposed workers and were positively associated with organochlorine exposure (Morgan, et al., 1980; Carlson & Kolmodin-Hedman, 1972).

Understandably, the liver is another organ which is particularly susceptible to pesticide exposure. A variety of effects have been demonstrated which were the result of exposures to different pesticides. The clinical severity of these lesions has ranged from liver microsomal changes (DDT and dieldrin) to angiosarcoma of the liver in agricultural workers spraying the Moselle Vineyards with arsenic (IARC Monograph, 1973).

The skin is also another organ which is particularly vulnerable to pesticide exposure. Skin lesions associated with occupational pesticide exposure include allergic and toxic dermatitis, chloracne and necrotizing exfoliative dermatitis. These several skin conditions, differing greatly in clinical severity, are illustrative of the spectrum of skin diseases which may be related to pesticide exposures.

Dermatologic lesions are the commonest of all pesticide related illnesses, and many can become chronic. Recently, in Dade County we found that 39% of serious pesticide illnesses were due to dermatitis.

In the genitourinary system, hemorrahagic cystitis has been linked to occupational exposure to chlordimeform (Folland et al., 1978) and renal tubular abnormalities to organophosphate exposures (Mann, et al., 1967).

Cancer Risks

No disease, is of more universal concern and interest than is cancer. The relationship of pesticides to cancer is the subject of continuing research, controversy and concern. Many of the pesticides which have been widely used in the past, have now been shown to be carcinogenic on the basis of animal testing and/or short term in vitro mutagenicity testing. In the U.S., several pesticides have either been cancelled or severely restricted in this connection, and to date the Environmental Protection Agency has issued Rebuttable Presumption Against Registration (RPAR) against 38 pesticides because an oncogenic risk was the trigger. Toxicologic data rather than epidemiologic data provided the evidence for the cancer trigger.

It is always difficult to extrapolate cancer risks from mice or rodents to man and good epidemiologic data, when available, is usually more acceptable and convincing because the risk in humans is measured. However, epidemiologic studies of pesticides for cancer risks are complicated by shortcomings in human exposure data, the multiplicity of pesticide exposures, changes in pesticide-use patterns, a rapid turnover of employees and the latency of cancer.

In spite of these difficulties, however, in the last decade a sizable body of epidemiologic data has appeared in the medical literature which is beginning to contribute to a better understanding of the carcinogenic risk to man of these chemicals. Most have been conducted in the occupationally exposed and clues have been provided in case reports, cross-sectional studies, case-control and cohort studies.

Epidemiological Studies of Insecticides - Retrospective Cohort Studies

In 1979(a), Wang and MacMahon pointed out that although there had been several clinical studies of workers occupationally exposed to insecticides, these were generally based upon small numbers, and had involved clinical and laboratory examinations; they commented on the fact that essentially no data could be found on the long-term mortality of exposed workers other than their study of workers during the manufacturing of chlordane and heptachlor (Wang and Grifferman, 1981).

Their study was a cohort study of 1,403 white male workers employed in the manufacture of chlordane and heptachlor (Wang and MacMahon, 1979b) who had worked for more than three months during the period of 1946-76. They found no overall excess deaths from cancer even in workers who had worked for 20 years or more. The 12 lung cancer deaths observed exceeded the 9 cases expected but the difference was not significant.

The manufacturing scene has also been the site of other occupational studies of pesticide workers. Ditraglia et al. (1981) conducted a retrospective mortality study of 2,100 workers employed for at least six months in four organochlorine pesticide manufacturing plants during the period of June 1964 to December 1976. The Standard Mortality Ratio (SMR) and 95% confidence intervals (c.i.) for all malignant neoplasms were 69 (95% c.i. 35-135), 91 (95% c.i. 33-198), 82 (95% c.i. 58-116), and 68 (95% c.i. 25-147) respectively for the four plants.

In the first plant, there were three deaths due to stomach cancer observed when only 0.09 were expected. In the three plants there were slight excesses of cancer of the esophagus (2 observed, 0.85 expected), cancer of the lymphatic and hematopoietic system (6 observed, 4.09 expected). In plants 1 and 2 which were the same plants that Wang and MacMahon noted a small increase in respiratory cancer, the combined observed deaths for respiratory cancer were 9 whereas 7.87 were expected. None of these excesses were statistically significant in any site.

In another study of cancer and occupational exposure sustained during the manufacture of inorganic arsenic, Mabuchi et al (1979-1980) provided evidence for a causal relationship between occupational exposure to inorganic arsenic and lung cancer. This was a retrospective morbidity and mortality study of men occupationally exposed to inorganic arsenic and other insecticides during the period 1946-1977. There were 1,050 participants. Twenty-three deaths from lung cancer represented statistically significant cases over the expected number ($p < 0.05$). The SMR for lung cancer among male production workers with heavy exposure to arsenicals increased with duration of exposures spanning 4-11 months up to 25+ years and increased from 0.94 to 27.5; thus a dose response effect was suggested for lung cancer mortality because of these increases with the length of arsenical exposure.

With the engineering advances that have been made in worker safety, most would agree that the pesticide exposures in this setting are much less than those acquired during the process of application and mixing. Wang and MacMahon looked at applicator exposure and cancer risks in 4,483 Structural Pest Control Operators (SPCO) and termite pest control operators employed three months or more between 1967-76. The insecticide exposure of the entire cohort of SPCOs were to organophosphates, carbamates, organochlorine insecticides, botanicals and fungicides. Termite control operators were primarily exposed to heptachlor and chlordane.

Three hundred eleven deaths were observed and 370.9 were expected, giving an overall Standard Mortality Ratio (SMR) of 84 (95% c.i. of 75-94); 54.3 cancers were observed with 65.2 being expected (95% c.i. 64-109), SMR's exceeded 100 for three types of cancer. For lung cancer the SMR was 115 (95% c.i. 77-170), for skin cancers the SMR was 173 (95% c.i. 63-473) and bladder cancer the SMR was 277 (95% c.i. 101-761). Only bladder cancer was of borderline significance. The slight excess of lung cancer in the SPCO's was not observed in the 138 deaths in the termite control cohort. Relatively few of the study subjects were followed for 10 years or more and none of those with lung cancer fell into this category. Only 15% of the person years were attributed to workers who had more than 5 years of employment, and all were observed for more than 10 years. No smoking histories were obtained from the study subjects.

Epidemiologic studies of herbicides

Recent epidemiologic studies suggest a limited carcinogenic risk of phenoxyacetic acid and chlorophenol herbicides with soft tissue sarcomas; both case report and case control studies have provided data in this area.

Case-Reports

The first indication that occupational exposure to phenoxy acid herbicides might be associated with an increased risk of soft tissue sarcoma was described by Hardell (1977). He discovered that five of seven patients with malignant mesenchymal tumors were forestry workers with confirmed exposure to phenoxy acids. The remaining two were indirectly exposed to these compounds because their work involved clearing phenoxy acid treated areas.

In another setting and at a later point in time, four cases of soft tissue sarcoma were identified among the 105 deaths in four industry cohorts of employees from manufacturing plants in the United States. Workers had been exposed to 2,4,5-T (2,4,5-trichlorophenoxyacetic acid), TCP (trichlorophenol) and TCDD (Honchar and Halperin, 1981; Cook, R.R., 1981; and Moses and Selikoff, 1981).

Two additional cases from another manufacturing plant were also documented by Johnson, et al., (1981). These were in a father and son. The father who had a liposarcoma of the thigh had sustained a prolonged occupational exposure in a plant which manufactured large amounts of chlorophenols, whereas the son, who died as a result of metastisizing fibrosarcomatous mesothelioma did not have a long latency period between his first exposure at the plant and the onset of the disease.

Soft tissue sarcoma was not the only type of malignancy identified in Swedish workers with herbicide exposure. In 1979, Hardell described a histologically confirmed malignant lymphoma in a patient who had an immense exposure to phenoxyacetic acid. In a pilot trial, Hardell and Sandstrom (1979) reported that 14 of 17 lymphoma patients acknowledged exposure to phenoxyacetic acids and chlorophenols.

Case control studies

Hardell's case reports (1977, 1981) suggesting an unexpectedly high frequency of mesenchymal tumors in persons occupationally exposed to phenoxyacetic acid herbicides prompted a case-control study of soft tissue sarcoma in forestry workers exposed to phenoxy acids and herbicides (Hardell and Sandstrom, 1978; 1979). The relative risk of exposure to both phenoxy acid and chlorophenols was 5.7 (95% confidence interval 2.9-11.3) and chlorophenols alone 6.6 (95% c.i. not stated). Only two patients and two controls had been exposed to herbicides not containing TCDD's so that the observed Relative Risks obtained for chlorophenoxy acids and chlorophenols could clearly have been caused by dioxins since all chlorophenols and 2,4,5-T contain chlorinated dibenzodioxins as an impurity.

Eriksson, et al. (1981) conducted a similar case control study in southern Sweden; 110 men aged 25-75, diagnosed as having soft tissue sarcomas between 1974-1978 were matched with two controls per case. The soft tissue sarcomas included 33 leiomyosarcomas, 19 malignant fibrous histiocytomas, 15 liposarcomas and 9 neurogenic sarcomas.

Very similar risk factors were obtained from this study of herbicide exposed workers from south Sweden. The relative risk from both types of herbicides was 5.1 (95% c.i. 2.5-10.4). The authors concluded the data showed that exposure to phenoxy acid may be a contributory factor in the development of soft tissue sarcoma and that the risk is not limited to phenoxy acids that may contain chlorinated dibenzodioxins and chlorinated dibenzofurans for the relative risk for exposure to non-dioxin containing herbicides was 4.2 (95% c.i. 1.3-14.5).

Later in 1981, Hardell et al, found increased risks of malignant lymphoma in workers exposed to the phenoxyacetic acid and chlorophenol herbicides.

Cohort studies - cancer mortality

Retrospective studies have been conducted by several investigators in workers with occupational exposures to 2,4,5-trichlorophenol, the precursor of 2,4,5-T, and in workers with excessive exposure to TCDD manifested by the occurrence of chloracne (Cook 1981a; Ott, 1980). Ott (1980) examined the mortality exposure of 709 U.S. workers in the 2,4,5-trichlorophenol plant.

The only documented cancer death was a case of lung cancer in a 63 year old man who had an 8 year history of occupational exposure to 2,4,5-T and was a heavy smoker.

In Cook's (1980) review of the mortality experience of 61 TCP workers, he found that three workers had died of cancer; one from an adenocarcinoma of unspecified site; one from a glioma; and one from a fibrosarcoma. None had a previous chloracne history. Cook concluded that the data suggested that TCDD was not a potential carcinogen because of the lack of any dose response relationship and because the latency period of 14 years was sufficient time to allow for the identification of a potential carcinogen.

However, Honchar and Halperin (1981) reviewed the Ott, et al., (1976), the Cook, et al., (1980) studies and the report by Zack and Suskind (1980) with special emphasis on soft tissue sarcomas. By combining the cases from the three cohorts studied together with one unpublished study by Zack, Honchar and Halperin found that of the 105 deaths, 3 (2.9%) were due to soft tissue sarcomas. Only a 0.07% incidence of death from this type of malignancy would have been expected in 1975 American males between the ages of 20 and 84 years.

Conclusions

In this review of the epidemiology of pesticides, we have looked at some of the chronic effects which have been documented. Evidence suggests that a variety of different diseases might be associated with long-term occupational exposure to pesticides. With regard to cancer, the data with the exception of inorganic arsenic insecticides, are presently insufficient for the evaluation of the carcinogenic risk of insecticides.

Insofar as herbicides are concerned, the several studies of railroad, forestry and agricultural workers in Sweden provided limited evidence of a carcinogenic risk from occupational exposure to the phenoxyacetic acids and chlorophenol herbicides and TCDD. Soft tissue sarcomas and malignant lymphomas are two types of cancer in urgent need of further epidemiologic studies.

Coggon and Acheson, 1982, have recently reviewed the question, "Do Phenoxy Herbicides Cause Cancer in Man?," they conclude that further research is urgently needed to confirm or refute the associations both positive and negative which have been demonstrated in the Scandinavian case control studies and observations among workers employed in the manufacturing of these products in the United States.

In the meantime, the lesson for agromedicine from these epidemiologic studies is clear. The total picture is still not generally known and is still unfolding. In these circumstances no one will question the fact that any excessive exposure is unwarranted, and good agromedical practices should strive for exposure minimization.

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Chapter 4

Toxicological and Environmental Implications of Pesticide Resistance - A Significant Agromedical Problem

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SUMMARY

This chapter presents an overview of the evolution, current scope and inter-relationships of pesticide resistance problems in both agriculture and public health and the associated toxicological and environmental implications. The problems illustrate the need to develop an agromedical approach to formulate successful pest management programs. Special comments are provided on the nature of operational problems and the necessity to incorporate rational use of pesticides with traditional methods of pest management which are ecologically and environmentally acceptable. A series of special recommendations are presented for consideration of officials who are responsible for developing integrated pest management programs for control of pest species of concern to agriculture and public health.

INTRODUCTION

The first agromedical problem is concerned with the constantly enlarging problem of pesticide resistance and as explained in Chapter 1, the multiplicity of pesticides which have been developed in an attempt to deal with the resistance problem. The term "resistance" was defined by the FAO Working Party of Experts on Resistance of Pests to Pesticides as "...a decreased response of a population of animal or plant species to a pesticide or a control agent as a result of their application" (FAO, 1967).

In contrast to the second and third agromedical problems which are direct manifestations of toxicology, pesticide resistance is a biological phenomenon which can be influenced to a large degree by operational factors within the control of local officials. The development of integrated pest management (IPM) strategies tailored to local conditions is considered essential for success in delaying the spread of resistance. Development of these strategies will require the cooperative efforts of government officials, physicians, toxicologists, entomologists, agronomists, ecologists and other appropriate skills to consider all possible procedures to incorporate in the program. Such strategies require the conduct of special surveys to detect and characterize the current status of resistance in the country and detailed studies of the ecology of the pest species and their associated parasites and predators as well as the use of a whole host of non-chemical techniques, supplemented where necessary by the advised and informed use of appropriate chemical pesticides.

The phenomenon of pesticide resistance is a grave threat to man's ability to produce an adequate quantity of food and simultaneously protect himself from the ravages of malaria, dengue fever, filariasis and other vector-borne diseases. The sphere of pesticide resistance is constantly enlarging on a worldwide basis, and can be reliably predicted to increase in severity and continue to be a significant problem for the foreseeable future. Although, ultimately man is probably powerless to eliminate the problem of resistance, there are a series of special actions that can be taken to reduce the magnitude of the problem and maximize the usefulness of pesticides considered essential to agriculture and public health programs. The purpose of this chapter is to comment on the scope of the problem and report on special defensive measures for prolonging the useful life of pesticides.

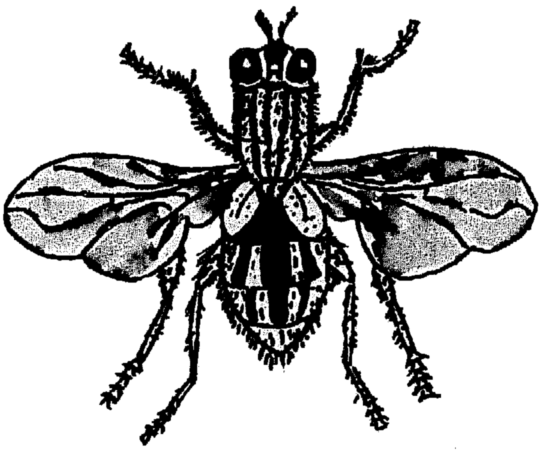
EVOLUTION OF THE RESISTANCE PROBLEM

The first case of acquired resistance of insects to insecticidal action appears to have occurred in the state of Washington in 1908 when the San Jose scale (Quadras pictiotus perniciosis) was found to be resistant to lime sulfur sprays (referred to by Brooks, 1974).

The first post World War II survey of the status of pest resistance to pesticides was made by Babers (1949). At that time he listed a number of references to resistance developed by a number of insects to hydrogen cyanide, arsencials, tartar emetic and phenothiazine. He also included references to DDT resistance in mosquitoes (Mosna, 1947) and houseflies (Missiroli, 1947). The Mosna reference is of special interest since the mosquito resistance occurred in the Latina Province of Italy, the site of some of the first field studies of the use of DDT for house-spraying for mosquitoes which took place in the spring of 1944. On the other hand, Missiroli referred to resistant houseflies in Naples, the site of the first massive use of 10% DDT dust for the control of epidemic typhus fever in the winter of 1943/44. Thus ample evidence was available as much as 30 years ago that resistance to DDT by both houseflies and mosquitoes could develop within 3 to 4 years. In a subsequent review of the status of the resistance problem (Babers, et al., 1951) many additional references are given to the status of housefly resistance to DDT, as well as resistance of filter flies, cockroaches, bedbugs, and bark beetles to DDT.

The problem was further exacerbated by the discovery that body lice in Korea were highly resistant to DDT (statement by A.D. Hess at a Conference on Insecticide Resistance and Insect Physiology (Anonymous, 1952)). This Conference was the first one of its kind to be called in the United States and was concerned primarily with the development of resistance by insects of medical importance. Although the recommendations of this first Conference were primarily concerned with realignment and extension of research on insect physiology and insecticide resistance the 8th and last recommendation recognized the fact that pesticides might not be the final answer and suggested "that fundamental studies on biological and ecological methods leading to naturalistic methods of control, including the use of parasites and disease organisms, be instituted and supported."

Nevertheless, primary emphasis continued to be placed on the search for pesticides which could be used for the control of resistant strains of both insects of public health and agricultural importance. In these early days, up to about 1960, DDT was used as the standard of comparison in terms of persistance, broad spectrum of effectiveness, cost and lack of acute toxicity and it is interesting to note that no other insecticide which could completely meet all of these criteria was ever discovered. Unfortunately we now realize that some of these characteristics, e.g. persistance and broad spectrum of effectiveness are generally undesirable although in certain cases persistance is desirable (i.e. for residual house spraying for malaria control). As more and more pesticides were discovered and brought into widespread use in the intervening years to combat resistance problems, particularly in the field of agriculture, serious difficulties were encountered with acute pesticide poisonings among users, since many of the newer compounds were more acutely toxic than DDT. Furthermore, the persistance characteristics of the organochlorine pesticides and their deleterious effects on non-target organisms and the environment generally became much more widely appreciated and understood.



The proliferation in the number of pesticides, their incorporation in mixtures to control resistance problems and sole dependence upon chemical pesticides has now resulted, in some areas, in the development of such high degrees of resistance that pests can no longer be economically controlled. Additionally, the general environment has been heavily contaminated with pesticide residues of some of the more persistent pesticides which can be expected to cause problems for many years to come.

Since the first indications of the development of resistance of pests to the synthetic organic pesticides in late 1947 and 1948, the subject has been of continuing and increasing concern both to international organizations such as WHO and FAO as well as to a number of the developed countries where such pesticides have come into wide-scale use. During the following years a number of surveys were made by various organizations to assess the extent and seriousness of the problem as presented in Table 4-1. Some of the earlier surveys were hampered by a lack of agreed methods of resistance assessment and in some instances at least, reported cases of resistance are based only upon laboratory data which was not confirmed by field experience.

Nevertheless, by the late 1960s the resistance problem had become so widespread that it was generally accepted as being inevitable and there was a marked decline in research on these problems and in the search for new chemicals for the control of resistant strains (Georghiou, 1980).

Table 4-1. Evolution of Number of Species of Insects and Mites Having Strains Resistant to the Synthetic Organic Pesticides.

Year	Agricultural Importance	Medical Importance	Total	Authority
1947	0	2	2	Babers, 1944
1951	1	5	6	Babers et al, 1951
1961	67	68	137	Brown, 1961
1965	200	--	200*	FAO, 1965
1976	225	139	364	Georghiou & Taylor, 1976
1980	262	152	414	Georghiou, 1980

*includes insects, mites, plant pathogens and rodents

CURRENT SCOPE OF THE RESISTANCE PROBLEM

Agricultural Aspects

The development of resistance in pests of field crops has been of special concern. In 1976, 33 species of cotton pests had developed resistance in comparison to a previous survey ten years earlier which revealed the development of resistance in 20 species (Reynolds, 1976). Selection pressures for development of resistance have been exceptionally harsh in many cotton producing areas of the world due to the extremely high quantity of pesticides used for control of pests.

Increase in resistance in pests of rice (excluding pests of stored rice) is similar to the increase for pests of cotton. In 1968, 8 species were reported as resistant to one or more insecticides and in 1975 the total had reached 14 species (Ibid).

Insecticide resistance in pests of field crops such as alfalfa, maize and sorghum has not been a serious problem in most areas. However, crop protection has been difficult in some areas due to the development of resistance in small numbers of major pests, particularly in development of resistance to organochlorine and cyclodiene insecticides by populations of the alfalfa weevil, *Hypera postica*, in the United States and U.S.S.R.; development of resistance to organophosphorus insecticides by the spotted alfalfa aphid, *Therioaphis maculata*, and in the cowpea aphid, *Aphis craccivora* in the U.S.A. and U.S.S.R., respectively; and resistance to organochlorine and organophosphorus insecticides by lygus bugs, especially *Lygus hesperus*, in alfalfa seed production (Ibid).

More recently resistance of plant pathogens to fungicides has become a serious problem. The fungicides for which resistance has been reported include the acylalanines, benzimidizols, dicarboximides, kasugamycin, pyrimidines and organic tins (Delp, 1981).

Detection and monitoring of resistance

By 1976 FAO had developed and published standardized test procedures for detection and monitoring of resistance in a series of agricultural pest species (Waterhouse, 1976) as follows:

a. stored food beetles
b. cocoa mirids
c. cattle tick larvae
d. sheep blowfly larvae
e. root maggot flies, carrot rust fly
f. rice stem borer
g. peach-potato aphid
h. green rice leafhopper
i. Egyptian cotton leafworm
j. Colorado potato beetles
k. codling moth
l. locust adults
m. sheep blowfly adults
n. spider mites

Early detection of resistance is especially important in the context of IPM programs because a change to another pesticide could be so disruptive to the biological control component of IPM that an entirely new program might have to be formulated (Georghiou, 1980).

Considerable progress has been made by FAO in recent years in expanding the list of standardized tests. Currently, 23 methods are available for detection and measurement of resistance in arthropod pests (insects, mites and cattle ticks) and 6 new tests are in preparation to characterize resistance in fungi.

Toxicological and environmental implications

As will be further discussed in Chapter 20, Regional Differences in Agromedical Problems, there are a number of toxicological and environmental implications associated with the resistance problem in agricultural pests. Whereas the acute toxicological hazard as indicated by mouse and rat LD50's to users of such pesticides as DDT, malathion, diazinon, and carbaryl are relatively low, resistance to such pesticides and the substitution of more acutely toxic pesticides such as parathion, dieldrin, endrin and heptachlor would be extremely hazardous under LDC conditions. On the other hand, resistance to the persistent organochlorine compounds (duration of activity two to five years--such as DDT, BHC, lindane, aldrin, dieldrin, endrin, chlordane, heptachlor) and and the substitution of such non-persistent compounds (duration of activity one to 12 weeks--such as malathion, methyl parathion, parathion (ethyl) and carbaryl) would not result in prolonged environmental contamination. (Ling et al., 1972).

Public Health Aspects

The World Health Organization (WHO) has provided exceptional leadership on a global basis for detection and subsequent monitoring of pesticide resistance of special concern to public health. In particular WHO publishes special reports on the status of insecticide resistance in various areas of the world. All persons who are interested in obtaining current information on resistance in a given country should consult appropriate WHO publications and official representatives of WHO who may be able to provide specialized advice to local authorities.

Pesticide resistance will continue to be a serious threat to the health of future generations as long as insecticides remain the principal tool for control of vector-borne diseases of man (Pal, 1976). In 1980 WHO echoed the same principal theme. The trends are clear and the list of resistant species is constantly growing on a global basis. The most significant new developments reported by WHO center around the appearance of multiresistance in several important vectors. The discovery of DDT resistance in the sandfly, *Phlebotomus paptasi* in Bihar State, India leaves the tsetse fly as the only important vector species in which resistance has not been reported.

The progressive spread of resistance to an increasing number of insecticides by an expanding number of vector species has impeded implementation of effective disease control programs. The following is a representative example of the impact of resistance on the ability of local authorities to control vectors of disease around the world.

Malaria vectors

The development of resistance in Anopheline species throughout the world has made control of vectors of malaria increasingly more difficult. Additionally, the cost of insecticides has complicated the issue. The change from persistent organochlorine insecticides of moderate cost to more expensive and less persistent organophosphate and carbamate insecticides has presented special difficulties. The impact of increased operational costs is yet to be fully appraised, but at the least it poses a serious threat to the future of control programs in many developing countries.

In Mexico and Central America, resistance has rapidly developed to most insecticides used for control of *Anopheles albimanus*. It would appear that the development of resistance in this species was accelerated by the agricultural use of pesticides in adjacent areas. In addition, the development of resistance in this species in Haiti to DDT has necessitated a change in some areas to organophosphates.

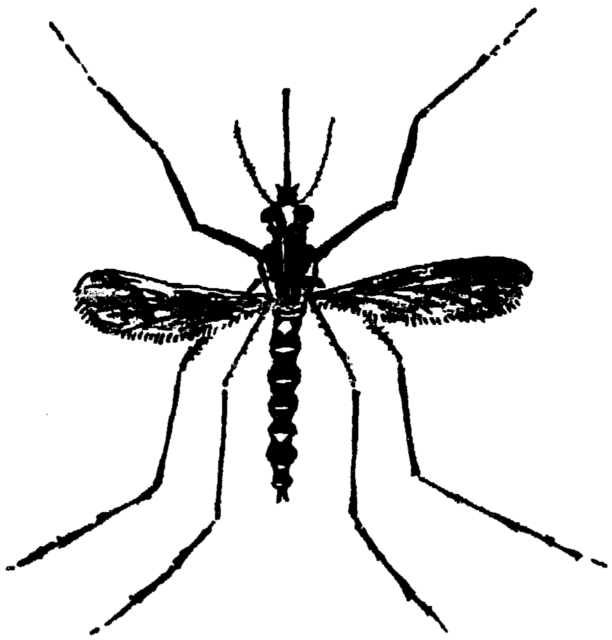
In Africa, resistance to organochlorine insecticides is rapidly expanding for the *Anopheles gambiae* complex as a result of agricultural practices. Thus malaria control programs will soon have to rely on use of intervention measures and insecticides other than organochlorines.

In South-East Asia, resistance is spreading and the continued use of organochlorines may be compromised in the near future. DDT is still being used in Burma for residual spraying in spite of documented resistance in *A. annularis* and *A. balbacensis*. In India, *A. culicifacies* is resistant to DDT, BHC and malathion in areas populated by approximately 250 million people. Additionally *Anopheles stephensi* is resistant to DDT in urban areas possessing populations in excess of 13 million of which about three million live in areas in which dual resistance to DDT and BHC has been reported. In Sri Lanka, malathion and fenitrothion were substituted for DDT and it was possible to achieve a dramatic reduction in the incidence of *Plasmodium falciparum* malaria.

In the Mediterranean, the spread of resistance to DDT and BHC has necessitated the conversion to malathion in Egypt, Iran, Iraq, Afghanistan, the Syrian Arab Republic and the Sudan. Although resistance is developing to malathion, control results are very effective wherever good coverage is obtained.

Other insect vectors of disease

Control of Culicine mosquitoes has been made more difficult and expensive due to development of resistance to a series of insecticides. Successful control of *Aedes aegypti* is now achieved by larviciding with temephos and adulticiding with malathion in most areas of the world. Lack of control of *Aedes aegypti* and associated severe outbreaks of dengue fever in Central America and the Caribbean have been attributed to the inadequacy of control meaures rather than to organophosphate resistance.



Detection and monitoring of resistance

The World Health Organization has developed standardized test procedures for all medically important pest groups. Test kits for susceptibility tests for larvae and adults are available. In addition, detailed instructions on how to conduct tests are provided in response to requests to WHO for information.

Toxicological and environmental implications

The toxicological and environmental implications associated with the resistance problem with public health pests are somewhat different from those associated with the resistance problems with agricultural pests, particularly as they relate to malaria control operations. The backbone of the malaria control program has, for many years depended upon application of DDT to the interior of human habitations on either a yearly or half yearly basis. Note that for this purpose, persistence is a desirable quality. Although this technique worked best in well constructed buildings providing only limited access to mosquitoes, it also worked exceptionally well in the more open types of construction found in tropical areas. Most Anopheline vectors of malaria are crepuscular and seek cool, shaded areas to rest during the day, only actively seeking a blood meal and either becoming infected with or transmitting malaria during the early evening hours, although there is a somewhat smaller peak of activity during the very early morning hours. Anopheles gambiae in Africa is a notable exception, being an active day-time biter.

As the resistance problem developed and expanded, a number of alternative pesticides were evaluated and field tested by various WHO field teams. Unfortunately, none of these newer compounds e.g. malathion, dieldrin, fenitrothion, chlorphoxur and propoxur were as persistent as DDT, all were more costly and some, more acutely toxic. The problem was further complicated by the fact that extensive toxicological data was necessary before these newer compounds could be applied to houses which might be occupied 24 hours a day by children, the sick and the aged.

Under these conditions a number of these newer compounds came into widespread agricultural use, where the toxicological implications were quite different, with the result that the Anopheline mosquitoes in these areas became resistant to the newer compounds before the compounds could be toxicologically cleared for routine house spraying. These interactions between agricultural and public health uses will be discussed further in the following section.

INTERRELATIONSHIPS BETWEEN AGRICULTURAL AND PUBLIC HEALTH USE OF PESTICIDES

We have been concerned for many years with the interrelationships between agricultural and public health use of pesticides, the first known reference to this possible interrelationship being pointed out by Dr. Richard W. Fay (Anon., 1952 pg 11) where he referred to the residual contamination from cotton spraying influencing the development of resistance by houseflies in South Texas. This concern was brought into focus when one of us (FW) was employed by the Pan American Health Organization (PAHO) to lead a team for the field evaluation of possible substitutes for DDT for malaria control in El Salvador in 1962. By that time, the previously highly successful malaria control program which had been initiated in the mid-1950s had collapsed to the point where the incidence of the disease had regained the level which had existed prior to the start of the program seven years earlier, primarily caused by the extensive use of a number of pesticides, including DDT in the surrounding cotton growing areas. This relationship between agricultural use of pesticides and the resurgence of malaria has recently been studied in much greater detail by Chapin and Wasserstrom (1981) in both India and Central America. These authors cite a study by ICAITI that cotton growers in Guatemala, Nicaragua and El Salvador have increased the number of annual applications to cotton from 8 or 9 times (in 1960) to as many as 50 in 1970 and further estimate that at current rates of application each kilo of insecticide added to the environment will generate 105 new cases of malaria.

These same authors also present data from India that as DDT use has increased from some 1 million kilograms in 1969 to 7 million kilograms in 1977, malaria cases have increased from about 500,000 to more than 30,000,000.

In the pre-World War II era the eminent malariologist, Hacket (1937) refers to a saying in Italy that "malaria flees before the plow" and cites a number of instances where malaria and a highly developed agriculture seem to be initially incompatible, not withstanding that in other places malaria persists in its severest forms in the face of an intensive cultivation of the soil. The latter situations have been further aggravated with the use of the new synthetic pesticides for agricultural purposes. It now appears in fact, that "malaria accompanies the plow." This situation has led A.I.D. to propose a policy for agricultural development, generally, that such activities must be undertaken in such a way that the incidence and prevalence of human disease is not exacerbated by agricultural development - a policy which was established many years ago in the United States in connection with the development of the Tennessee Valley Authority.

MANAGEMENT OF PESTICIDE RESISTANCE PROBLEMS

The management of pesticide resistance problems is completely dependent upon the management of pesticides. Thus in those countries where there is little or no regulatory control over the importation, distribution and use of pesticides (including disposal of unused pesticides and pesticide containers) and pesticides are widely used for many different purposes without adequate consideration for their acute toxicological hazards as well as their impact on the general environment, pesticide resistance problems will inevitably arise. Accordingly the first step towards management of pesticide resistance problems must be the creation of an awareness of these problems and their interrelationships between agricultural and public health pest control problems in the minds of government officials, the farming community and the general public.

Early attempts at management of the pesticide resistance problem were limited by insufficient knowledge of its genetic nature, the mode of action of insecticides and detoxification mechanisms and mechanism of resistance in their biochemical, morphological and behavioristic aspects--See recommendations of the Conference on Insecticide Resistance and Insect Physiology (Anon., 1952). These early attempts at management of pesticide resistance were also limited by the relatively small number of pesticides available at that time; DDT, chlordane, lindane, and dieldrin, all of which were more or less persistent. Thus alternation of pesticides as a means of delaying the development of resistance was not feasible, at least for residual spraying for housefly and mosquito control because residues of previously applied pesticide would still be active (Anon., 1952, pg 11). However, enough information was available at that time to conclude that treatment of both larval and adult stages (of houseflies) greatly intensifies natural selection and inbreeding and hastens the development of resistance (to DDT) (Anon., 1952, pg 27).

In those early days, also, field control personnel found it very difficult to believe that resistance (to DDT) had, in fact, developed and the usual response was to increase the rate of application and decrease the interval between applications. Such tactics further increase the selection pressure and accelerate the development of resistance problems as does any excessive, over-use of pesticides.

From 1952, up to the late 1960s there was great interest in the problems of insecticide resistance, reaching a peak in 1958 when approximately nine percent of the papers published in the Journal of Economic Entomology were concerned directly with insecticide resistance (Georghiou, 1980). From the late 1960s through the early 1970s, this interest, as reflected in published scientific papers as well as numbers of compounds cleared through Stage I of the WHO insecticide testing program showed a marked decline and was accompanied by an attitude of "inevitability" i.e. that resistance problems of chemicals were unsolvable (Ibid).

In recent years, however, with the growing interest in integrated pest management (IPM) and the realization that in most instances the judicious and timely use of appropriate narrow spectrum non-persistent pesticides, are an essential component of IPM programs, there has been a revival of interest in the resistance problem.

Georghiou (1980) in his recent paper on the "Management of Insecticide Resistance" discusses a number of genetic and biological factors influencing the selection and resistance to insecticides in field populations and concludes that "The greatest opportunities for countering the phenomenom of resistance lie in our ability to limit the degree of selection pressure according to the propensity for resistance of the target population." He concludes "...that resistance would be delayed the most or may be avoided entirely if the following conditions were fulfilled:

> (a) the pesticide has short chemical stability i.e. non-persistent (b) is not related to an earlier used chemical with respect to mode of action or metabolism (c) the formulation does not provide prolonged release of the chemical in the environment (d) the percentage of the total population killed is relatively low (e) use of the chemical is directed mainly against adults (f) the application is localized rather than area-wide and (g) certain generations are left untreated.

While the simultaneous use of all of these measures may be impractical for many field problems, they hold promise for delaying the development of resistance in the context of integrated pest management programs provided that the necessity for pesticide managment is recognized and can be effectively implemented at the national level.

Somewhat similar strategies for handling fungicide resistance problems are described by Delp (1981).

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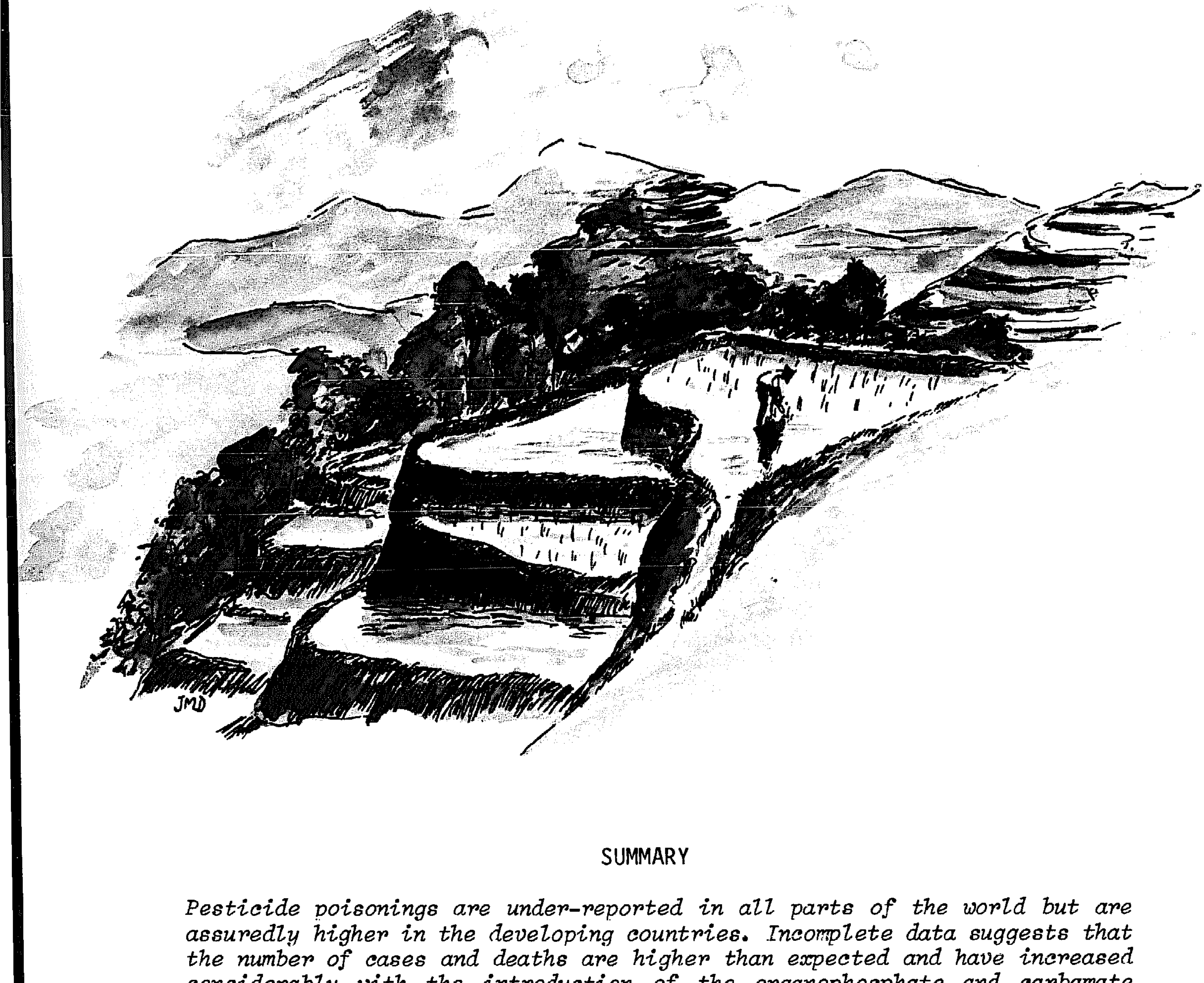
PART II

PREVENTION, DIAGNOSIS AND TREATMENT OF PESTICIDE POISONING

Chapter 5

Pesticide Poisonings--Who Gets Poisoned and Why?

Davies, J.E.



SUMMARY

Pesticide poisonings are under-reported in all parts of the world but are assuredly higher in the developing countries. Incomplete data suggests that the number of cases and deaths are higher than expected and have increased considerably with the introduction of the organophosphate and carbamate insecticides to the different areas of the Third World.

This Chapter reviews pesticide poisonings, a problem which is of equal concern to agriculture and public health and one which constitutes a major agromedical problem. Mechanisms of poisonings and potentially hazardous situations are discussed.

INTRODUCTION

Past experience has shown that whenever there is increased use of agricultural chemicals human pesticide poisoning soon becomes a major public health problem. This has particularly true when organophosphate pesticide usage supercedes organochlorine usage.

Human pesticide poisonings are the most severe adverse health effects of pesticide exposure and most cases are usually preventable. With current pesticide management policies, the organophosphate and carbamate insecticides are the chemical groups most frequently involved so that cholinergic illness is the most frequent manifestation of intoxication. Although absorption may occur through ingestion, inhalation, or via the dermal route, most occupational poisonings are due to dermal absorption.

In Dade County, Florida in 1977, we investigated some 121 suspected poisoning incidents, but were only able to confirm 51 (42%) of these by subsequent clinical and laboratory investigations. The data emphasizes how difficult it is to obtain a true measurement of the magnitude of the pesticide poisoning problem because everything that is called a pesticide poisoning is not necessarily so.

Poisoning Incidence

Pesticide poisoning statistics are very important for those who have to plan importation and pesticide control programs in a country. The data provide valuable information on what chemicals can be safely imported and which can be registered or re-registered in the individual country.

In most areas of the world nobody knows how many pesticide poisonings are occurring. Neither the doctor, the clinic staff, or even the farmer are officially required to report that a person has sustained a pesticide poisoning.

Just to illustrate how widespread is the problem of under-reporting, even in highly organized areas of pesticide management, such as exists in California, some still question the true magnitude of the problem. California is the only State where physicians treating pesticide-related illnesses must notify the California Department of Agriculture to receive their reimbursement for services rendered (Cal. Ag. Code, 1970). In that State, in 1973, 1974, and 1975 officials reported that there were: 1,474, 1,157 and 1,343 cases respectively. A further breakdown of the 1,343 cases occurring in 1975 showed that 39% were classified as sytemic poisonings, 35% skin diseases, 23% pesticide-related eye injuries and a miscellaneous 5% for other illnesses (Maddy and Peoples, 1976).

Who Gets Poisoned and Why?

The likely victim of a pesticide poisoning will be somewhat different in a developing country as compared to a developed country. This is because there are important differences relating to the method of pesticide management practices in different countries and in the overall level of training and understanding of pesticide toxicity. These have a bearing on the qualitative and quantitative characteristics of pesticide poisoning. Field visits have taught us that poisonings often occur in the most unexpected of circumstances and we shall describe some episodes which were encountered in different parts of the world in order to emphasize these unexpected circumstances which so often are contributory to the misuse of pesticide and are indicative of the misunderstanding of pesticide toxicity.

Poisoning Problems in the United States

In the United States only 10 years ago the pesticide poisoning position was serious; many deaths were occurring. Some now believe that the situation has improved because there are fewer reports of serious poisonings and fatalities. This favorable trend has been due to the use of less toxic pesticides, applicator training programs, and the better recognition and management of poisonings by doctors and nurses in the emergency room. Milder illnesses, however, are still very common and the three population sub-groups at special risk of poisoning are:

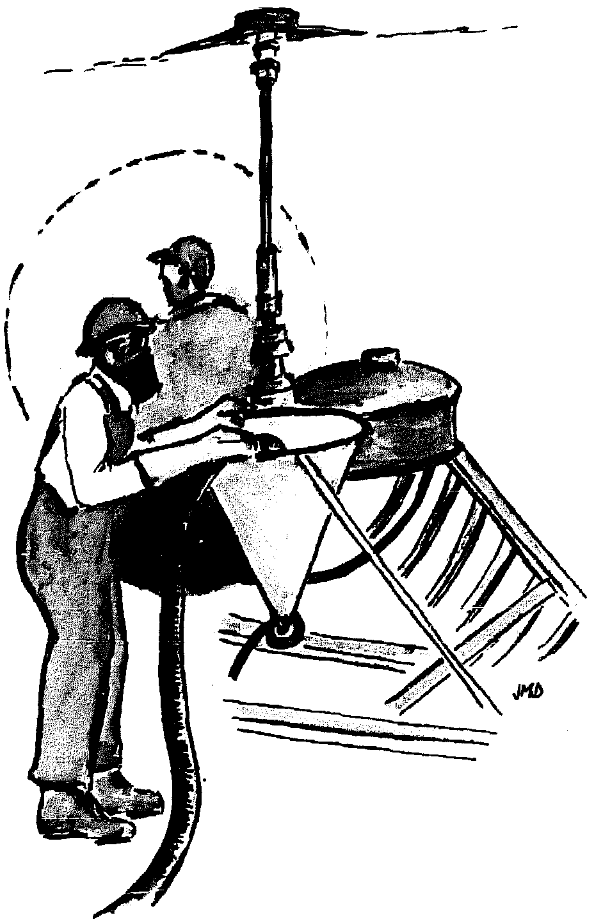
1. mixers, loaders and applicators;
2. pickers and thinners; and
3. the general population, especially a child.

Applicator and Mixer-Loader Poisoning

Applicator poisoning occurs as a result of a worker's exposure to the pesticide concentrate. Hazards exist both from the process of mixing and diluting the concentrate when accidental spillage may occur, and during the process of application as a result of drift and saturation of clothing. On most occasions, exposure is the result of dermal absorption although inhalation of dust and powder from disintegrating granules poses a risk of poisoning from inhalation also. These are the reasons why full protective clothing should always be worn during the mixing and application of pesticides. The types of protection afforded by the wearing of these are further described in Chapter 12; the methods of minimizing applicator-mixer exposures through correct application techniques are described in Chapter 13.

Clinically these cases are more serious than those seen with the syndrome called "picker poisoning" and workers mixing and applying the more toxic pesticides need to be properly trained and should receive regular monthly cholinesterase testing (Federal Working Group, 1974).

Workers associated with the aerial application of pesticides are especially highly exposed. It is unwise for a pilot to mix and load chemicals. The normal procedure is to employ aircraft loaders and swampers, whose job is to dilute the material and load the aircraft before each run. This is done on the airstrip with fixed wing aircraft. Helicopters are often loaded from an accompanying trailer at the scene of application. Loaders are one of the most highly exposed occupational groups in the entire mixer/loader application process.



An example of applicator mixer/loader poisoning was Tony B., who was employed as a pesticide mixer/loader for a helicopter crop dusting firm. He started loading the aircraft at 6:00 a.m. with a mixture of ethyl/methyl parathion 6-3, toxaphene and methomyl.

He soon began to feel unwell. He was admitted at 11:35 a.m. to the emergency room of the local hospital. He complained of nausea, vomiting, weakness and blurring of vision. His pupils were constricted and there was profuse perspiration. A screening cholinesterase test revealed severe inhibition. He had not realized that his clothing had become saturated in the chemicals. After being put in a shower and scrubbed all over, he was given a total of 12 mg of atropine intravenously in the emergency room over a brief period of time then oxime 2-PAM was also administered in one gram dose of 1,000 cc of D5W. Atropine therapy was continued after his transfer to the medical ward and he proceeded to improve over the next few days.

Subsequent blood and urine metabolites studies by the laboratory confirmed that the poisoning was due to ethyl and methyl parathion.

The special lessons of this case are: (1) the illness was severe, (2) there was no positive history of an accidental spill, and (3) only one applicator was affected.

Picker poisoning

Once a pesticide has been applied to the crop, the diluted pesticide residue remains on the leaf, fruit or flower for a varied period of time. This residue is called a dislogable residue because it can be brushed off by the wind or by mechanical factors such as the disturbance caused by a worker's arm pushing through the leaves to get to the crop or fruit. The concentration of pesticides in the foliar residue declines with the passage of time as a result of biodegradation and photochemical action. This is the basis for the establishment of re-entry intervals in the United States (DOL, 1973). This interval, which is printed on the label and should be posted in the field after application, is the time which must elapse before a farmer can allow his pickers to go back into the field after pesticide spraying.

Floriculture

Weather (especially rain) affects the rate of dissipation and, in addition, high temperatures sometimes convert the pesticide into a more toxic breakdown product. Premature entry to a treated site poses a hazard for the worker and produces multiple illnesses. Most frequently this has been observed in workers picking either citrus, peaches or grapes where there is an abundant leaf canopy; it may also occur in floriculture where the worker may sustain significant dermal exposure during the thinning and banding of flowers. Similarly, in apple orchards, workers may be exposed during the thinning process.

Mention should be made of two types of pesticide workers who are at special risk of intoxication, the first is called a "scout." This person regularly goes into the fields to count the number of pests on the plants. Since the job often involves going into the field shortly after application, there is a special risk of residue intoxication.

The second worker who is at special risk from pesticide application is the "flagman." He stands at the end of the field with a flag to indicate where the aerial applicator should cutoff the spray and start climbing, the flagman marks the end of the application and often gets covered with spray. It is easy to see why this person is at risk of excessive [illegible]ure and un[illegible]tunately he is usually unprotected by the necessary prot[illegible]

Cotton is a crop with a large leaf surface but it is almost entirely machine harvested in the U.S., so that residue poisoning is not a serious threat with this crop. This is not the case however, for Central America, where hand harvesting is still practiced and hundreds of cases of "picker poisoning" have been reported. The following outbreak, which actually occurred, is typical of a picker poisoning episode.

An emergency room nurse realized that she had 3 patients with mild symptoms resembling what she had been told about organophosphate poisoning. She found 3 more patients in the Waiting Room with similar symptoms, and learned that 4 more were on their way to the hospital. Reports indicated that all were weak, sweating and complaining of abdominal cramps, nausea and vomiting. On examination the nurse noted that most had very small miotic pupils.

By the end of the evening, 10 of a crew of 17 migrant workers who had been detasseling corn that morning had been admitted to the hospital.

Picker Poisonings at the Emergency Room

Each had received atropine and by the end of the day most cases were responding and there were no fatalities.

Further interrogation revealed that the group had entered a cornfield after an airplane had sprayed the field with methomyl. Their clothes and canvas shoes had become moist from the dew on the ground and from the moisture on the leaves. In this way they had sustained a dermal residue intoxication.

Pesticide Poisoning in the U.S. General Population - The Magnitude of the Problem

At present the amount of pesticides being produced in the United States is 1.6 billion pounds per annum. In 1973, 49% of the total products were insecticides, 39% were herbicides and approximately 12% were fungicides. Since then herbicide production and usage has increased. In addition, some- [illegible] in the [illegible]n of 1 million pounds of petroleum oils, synthetic sprays and other petroleum products are used as diluents or carriers of pesticides, a fairly important statistic if one remembers the propensity of these materials to produce rashes and skin conditions. The U.S. Environmental Protection Agency estimated "that 2,831 individuals are hospitalized every year (US EPA 1976)," and, in addition, there are approximately 12,220 emergency room cases of pesticide poisoning annually based on statistics from the U.S. Consumer Product Safety (CPSC, 1976).

Examples of Misuse

As is the case with all Poison Control Center statistics, the toddler or young infant represents the person at greatest risk. Examples of some dangerous situations, typical of misuse which we have encountered, include the following:

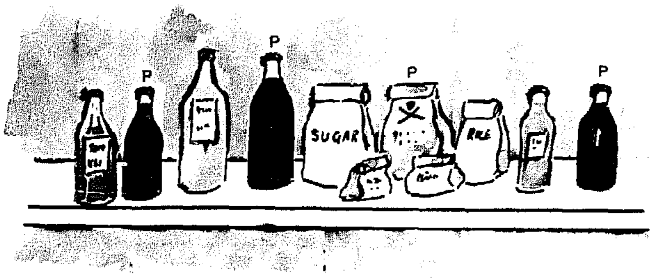
1. placing highly toxic pesticides in soft drink or beer bottles,
2. placing pesticides alongside food in the kitchen,
3. the use of warfarin and roach powders or liquids which are placed within easy reach of the child,
4. disposal of half-empty pesticide drums in garbage dumps which may be picked up by children and cause subsequent poisoning, and
5. milky pesticides and geophagia (soil eating) - we have seen several serious poisonings in infants where the babies were poisoned after being fed pesticides because the mothers had mistaken the white pesticide solution for milk. Some pesticide solutions turn milky when water is added, and on one occasion this was actually stored in the refrigerator!

The young toddler should not be taken to the field when the mother is working there. It has been found that children, especially those suffering from anemia or malnutrition, frequently take to eating dirt; this habit, which is called geophagia is common, and the following was a case which occurred as a result of this habit:

A 3-year-old child was taken to a local migrant clinic with extreme miosis, foaming at the mouth and nose, and diffuse rales throughout both lung fields. An exposure history revealed that the field had been heavily treated within the last 3 days with mevinphos (Phosdrin®), Kelthane,® and parathion. Chemical analysis showed cholinesterase inhibition. Parathion was identified in the gastric contents. It was later determined that the intoxication was the result of ingestion of soil containing parathion.

SOME PESTICIDE DON'TS

Don't place highly toxic pesticides in soft drink or beer bottles



Don't place pesticides alongside food in the kitchen

Don't place warfarin and roach powders or liquids within easy reach of the child

Don't dispose of half-empty pesticide drums in garbage dumps

PESTICIDE POISONING PICTURE IN DEVELOPING COUNTRIES

When one tries to review the how, the why and the wherefore of pesticide poisoning in the developing countries, it soon becomes apparent that there are a lot of factors contributing to the problem.

Numbers of Cases

The first thing that strikes one is the number of poisonings. Although there are no solid data it is clear that a lot of people in rural areas are getting poisoned. There is an urgent need to monitor this to find out how many, why, and how can the poisonings be prevented.

Situational Factors

The second factor is situational. In the past in these areas, the applicator had been accustomed to using DDT. He had found it safe and illness had not been associated with application. With the introduction of the newer and more toxic organophosphates he was totally unprepared for the potential of these newer chemicals which were replacing DDT. Mention should be made in regards to the situation that exists in the emergency rooms in many rural hospitals in many Third World countries. Here doctors and nurses have seldom received special training to recognize, treat and prevent acute pesticide poisonings. The same is true for the graduating medical student, for final examinations rarely include questions on the topic of pesticide poisoning.

Hazardous and Risky Areas

The several potentially hazardous situations which may occur can frequently be anticipated by looking at the distribution systems by which chemicals enter and move through a country.

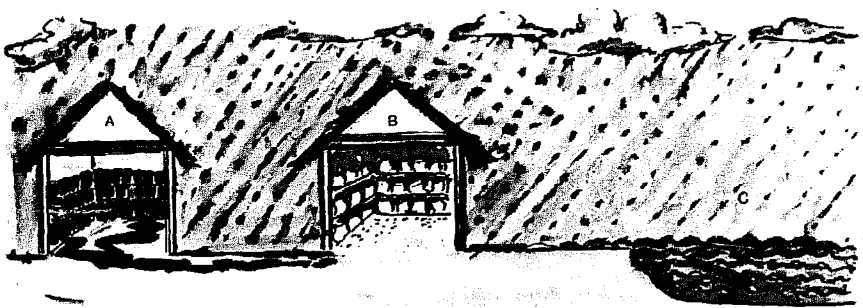
The Dockside

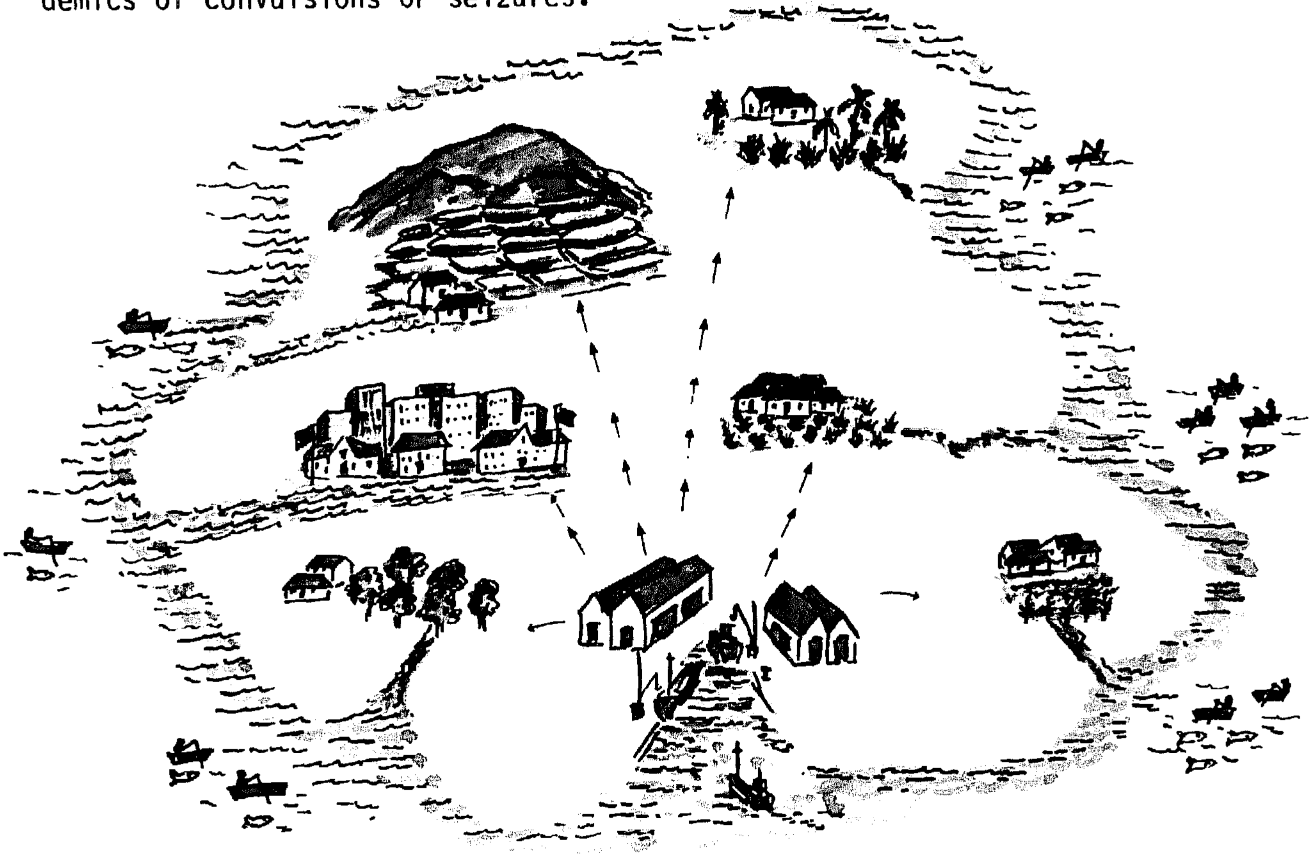
Very little manufacturing is done in the Third World countries so the first locale of potential hazard is the port, where active ingredients are unloaded off the ship. Several episodes have been documented wherein spills have occurred either while the ship was at sea or at the time of unloading at the dockside. The latter situation is especially hazardous if pesticide drums are not handled with care; they can be ruptured or perforated by a forklift and contaminate the environment or the dockside personnel.

Often stevedores have to unload a cargo without first seeing the manifest and determining whether the cargo contains toxic chemicals. Chemicals need to be stored in containers which can be recognized by color codes. These are some issues which labor and agriculture could contribute to improved worker safety insofar as pesticides are concerned.

The Risks During Formulation, Transportation and Storage

From the ship the drums are moved to dockside warehouse or to storage facilities adjoining formulation sites. Both sites are areas of potential hazard, and storage facilities for pesticide warehouses vary enormously in different parts of the world. Some sites are newly constructed concrete buildings with excellent ventilation and drainage facilities, with the pesticide drums stored under lock and key and with excellent drum rinsing or drum disposal facilities. In other areas, drums may be piled up on top of each other on the dirt floor. When there is heavy rain, such as occurs during the monsoon season, pesticide puddles lying on the floor may be washed down the road to an adjoining warehouse where rice or flour is being stored in sacks. It is easy to see how pesticide poisoning can occur miles away from the actual site where contamination occurred. There have been reports where contaminated flour has been shipped to remote areas of the country and then subsequently causing epidemics of convulsions or seizures.

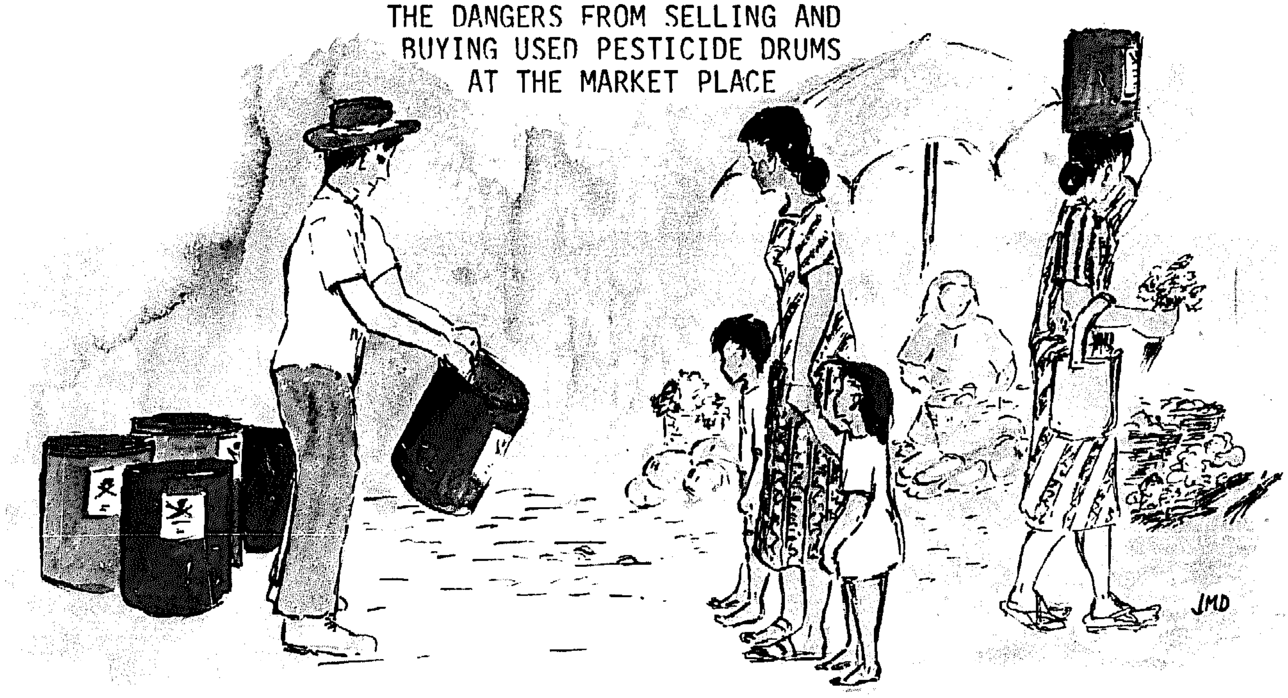




The formulating plant which is the next potentially hazardous site represents an especially dangerous situation and one in which there is an urgent need for close supervision and inspection. Here the concentrated active ingredient is diluted with solvents, carriers and other materials; it is then labeled and distributed to the user. In the past, in some formulating plants, empty beer bottles or soft drink bottles have been used for terminal dispensing of the merchandise, a practice which obviously places the user and his family at great risk.

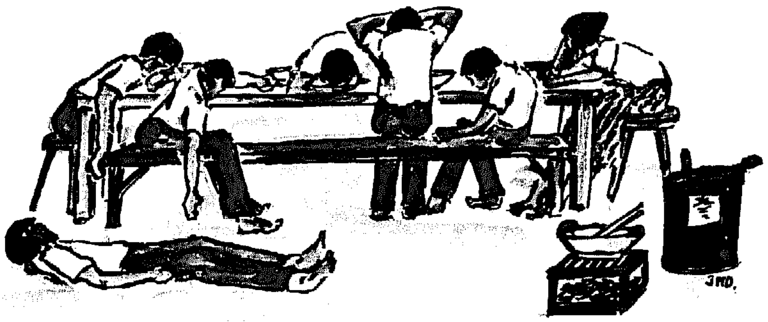
In many countries there are no requirements for licensing of pesticide shops, ubiquitously, the pesticide shop poses an especially hazardous spot, and it is where these bottles of chemicals are sold to the general public. It is not uncommon to see highly toxic materials such as ethyl parathion and endrin sold alongside food and cosmetics.

THE DANGERS FROM SELLING AND BUYING USED PESTICIDE DRUMS AT THE MARKET PLACE



Don't sell used contaminated drums *Don't buy used drums*

Don't store food in drums

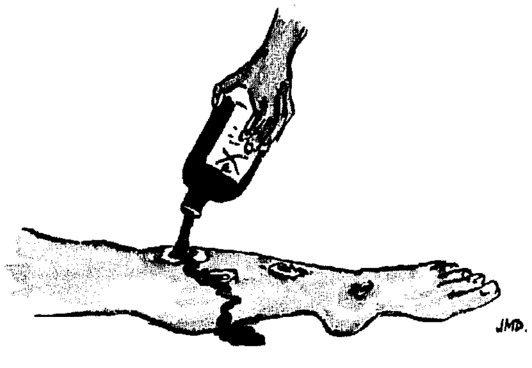


The unhappy outcome of contaminated food and it is where these bottles of chemicals are sold to the general public. It is not uncommon to see highly toxic materials such as ethyl parathion and endrin sold alongside food and cosmetics.

Hazards to the Consumer

Finally, potentially hazardous situations can be quickly recognized at the consumer level both at the urban and rural setting. Some of these are due to misunderstanding and others due to misuse. This writer (Davies, 1972), during a visit to the Far East for The World Health Organization with the objective of ascertaining hazards to man from pesticides, was informed that highly toxic pesticides were being poured into ponds to catch fish. The dead fish were sold later at the local market; when questioning a group of 35 persons about this practice, two farmers and two children readily admitted to using this technique and another farmer when interrogated replied, "Why certainly, how else do you catch fish?"

Several investigators have stressed the special contributions of semantics to pesticide misuse and misunderstanding. Thus, in Honduras, Wegland and Yaeger (1980), drew attention to the point that the word used in that country for any chemical which is construed to be very beneficial to plants or animals was "medicine." This obviously predisposes to the concept that pesticides might be misconstrued as being therapeutic and might be used therapeutically by the misinformed. A good example was seen in the Jakarta News in August 1969 which described four deaths in Samban because a grandfather treated himself and his three grandchildren with topical endrin on account of the family's problem with dermatitis.



Misuse is still common in many parts of the world and could lead to widespread pesticide contamination of food. Two serious examples of food

PESTICIDE MISUSE!

Pesticides have been poured into fish ponds.

The dead and dying fish are easily caught.

They are then sold in the market.

All who eat will be poisoned.

contamination with endrin are described because the events which took place caused many deaths and were typical of the dire consequences of population who were unaware of the toxicity of pesticides.

The sale and purchase of used pesticide drums is a very dangerous practice because it may result in serious food contamination:

> *Used pesticide drums had been purchased at the local market and then used to mix flour at a wedding at which numerous villagers had attended. The village head became ill and died; shortly thereafter his wife too succumbed. Several other people in the adjoining home also became ill and some died. All had eaten the same food because they had attended a communal feast which had been organized by two families. All had been served rice. The village nurse faced with this epidemic immediately mustered transportation sending the most serious cases to the hospital, and treating others at home with charcoal. By 5:00 a.m. the next day, 8 cases had been admitted to the local hospital and 4 others had died on the way to the hospital. Altogether 124 poisonings had occurred. Food from the two homes where the food had been cooked were collected by the Police Department and subsequent analysis confirmed that endrin was identified in samples of flour.*

Sweeping rice and sweeping flour is another common method of pesticide food contamination. Sacks of rice are sometimes transported in the same truck with an insecticide. Also, these rice sacks are sometimes perforated at the bottom end so that there is a small trickle of rice that runs out of the bottom. These discarded grains of rice are sometimes swept up, collected and sold as "sweeping rice." This rice is recognized as being inferior, and occasionally is contaminated with pesticides. As will be seen from the case study, such an eventuality caused serious poisoning to a physician and his family.

> *Dr. V. was a 48-year-old ophthalmologist who at 6:30 p.m. had supper with his wife and 18- and 14-year-old daughters. They had moved to a new house and Mrs. V. later reported that they had some endrin in the home and that the night in question they had used cheap flour and "sweeping rice." By 7 P.m. Dr. V. was called to see his eldest daughter and found her having convulsive seizures. The second daughter was talking on the telephone when suddenly she too collapsed. At the same time Mrs. V. also became sick and collapsed. Dr. V. then rushed to the hospital to get phenobarbital; he telephoned a physician colleague*

> *assistance; the hospital was only two blocks away. While treating his daughter with phenobarbital he too collapsed. When his physician colleague arrived he found all four convulsing and rushed them to the hospital. They were stuperous and having short seizures.*
>
> *All patients had gastric lavage and intravenous glucose and water. Phenobarbital 300 mg and 25 mg. of chlorpromazine were administered. The gastric washings from Dr. V. were sent to the capitol where endrin was subsequently identified. The attending physician noted that the pattern of the seizures were as follows: the stretching of all four limbs with hyperextension, arching the back, bending and turning the head to the right which was followed by a jerking expiratory scream. There was profuse frothing from the mouth but no cyanosis. Dr. V. had no memory of this period nor of giving his daughters phenobarbital. All four remained semi-stuperous for 24 hours but were later able to be discharged on the second and third day.*

With happenings such as have just been described, it is easy to see why governments in many parts of the world are reacting to these serious environmental problems.

In 1972, the Ministers of Health (Document No. 119) of the Americas met together to draw up a ten-year plan for the Americas. One of the significant recommendations was the unanimous resolution of "endeavor during this decade to reduce all intoxications and human deaths caused by the indiscriminate use of pesticides." This sentiment is one which is shared by developed and developing countries alike. The problem has arisen because pesticide safety has not been simultaneously transferred with the technology itself, so that there is a sizeable infrastructure in agriculture and health who are in urgent need of training. It is here that agromedicine has a major responsibility for future pesticide management programs.

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CHAPTER 6

Pesticide Toxicity and Mode of Action

Levine, R.S. and Davies, J.E.

SUMMARY

Principles relating to questions of pesticide hazard as compared with pesticide toxicity are briefly discussed and pathophysiologic mechanisms of selected important pesticides are presented.

INTRODUCTION

In earlier chapters on the chemistry of pesticides, mention was made of the need to differentiate the hazard from the toxicity of a chemical. The concept of hazard is by no means a uniform one, and it is easy to see why different interpretations and weighing of hazards are used by different disciplines.

From a chemical point of view, some important attributes of hazard are linked with the physicochemical properties of an agent. From a toxicological and hygienic point of view, the route of exposure, the methods of use, and the inherent toxicity of the chemical, are all important variables. For the public health physician, methods of application and usage, the comfort of protective clothing, the literacy and basic understanding of pesticide management by the pesticide infrastructure together with the cultural, psychological and behavioral attributes of the work force are all components of pesticide hazard.

In this chapter issues of pesticide hazard and toxicity are briefly discussed. Three fundamental principles of toxicology need to be emphasized at the outset:

(1) all chemicals, whether natural or synthetic, can be toxic if given in large enough doses and over sufficient periods of time,

(2) unless the chemical in question reaches a vulnerable site, no toxic effect will occur,

(3) as the dose of the chemical increases, so does the toxic effect increase.

The first of these principles cautions respect for even "innocuous" pesticides. The second and third principles provide specific directions for preventive activities, specifically minimization of unnecessary contact as well as unnecessarily high concentrations of pesticides; together, these principles may be utilized to reduce the hazards of exposure, even when dealing with very toxic pesticides.

INHERENT PESTICIDE TOXICITY AND DOSE RESPONSE CONSIDERATIONS

A simple animal test may be used to rank pesticides with regard to inherent toxicity. Before pesticides are registered and released for public use, the manufacturer must declare the LD50 of the chemical, (i.e., how much of the chemical is necessary to kill 50% of the test species, usually the laboratory rat). The LD50 is measured in terms of oral (ingested), dermal (topical), and respiratory (inhaled) toxicity. Figures 6-1 and 6-2 exemplify the results of such ranking for some organophosphate and organochlorine pesticides. The materials on the top of the list are the most toxic and those at the bottom the least toxic.

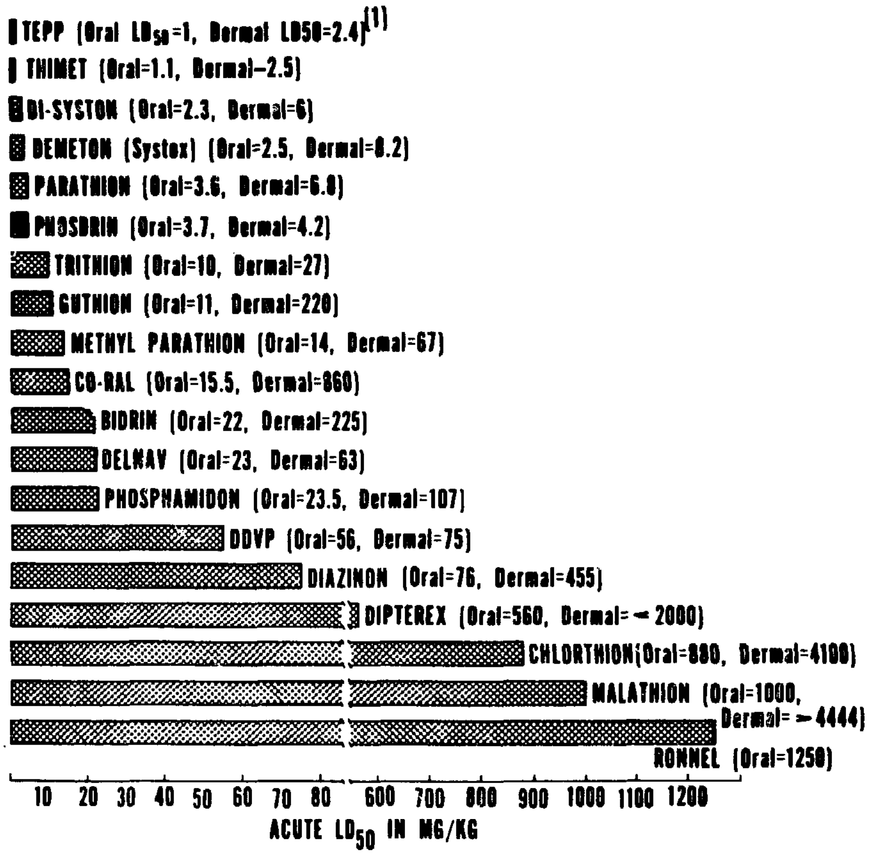

Figure 6-1. *Acute Oral and Dermal Toxicity Values for Some Organophosphate Pesticides*
(Prepared by the Bureau of Occupational Health, State of California Department of Health. Copied with Permission.)

Actual statistics of human poisoning correlate reasonably well with such toxicity ratings. In general, the acute oral LD50 is mg/kg dose of the technical material which will kill an adult human is as follows:

Acute Oral LD50	Material Which Will Kill an Adult Male
5	a few drops
5 - 50	a pinch or 1 teaspoon
50 - 500	a teaspoon or tablespoon
500 - 5,000	1 ounce to 1 pint (1 pound)
5,000 - 15,000	1 pint to 1 quart

Despite the unifying features of biochemistry and physiology for classes of organisms, peculiarities of species, even individual members of a population, determine the response to a given amount of chemical. In general, however, if each member of a test group simultaneously receives larger doses, then an increasing number of animals will be affected as the dose increases. Thus, at a low dose, one or more individuals will exhibit a response that can be measured. If the response is considered harmful to the organism, the dose that just produces the effect is called the toxic threshold (Hayes, 1963). Dose levels below this are termed "no observable effect level." As the dose increases, the number of individuals affected also increases until eventually virtually every one of the members of the groups respond. This gives a skewed dose/response curve that may be transformed into a straight line form by an appropriate choice of graphic presentations, i.e., the one which considers the statistically reliable measure is the median level--the dose which provides or causes the response in 50% of the individuals.

It is important to remember that no matter how toxic the chemical, there will be no effect if there is no exposure. Thus, if the level of exposure is minimized, the effect will also be minimal or non-observable. It is important that all who handle pesticides understand this principle.

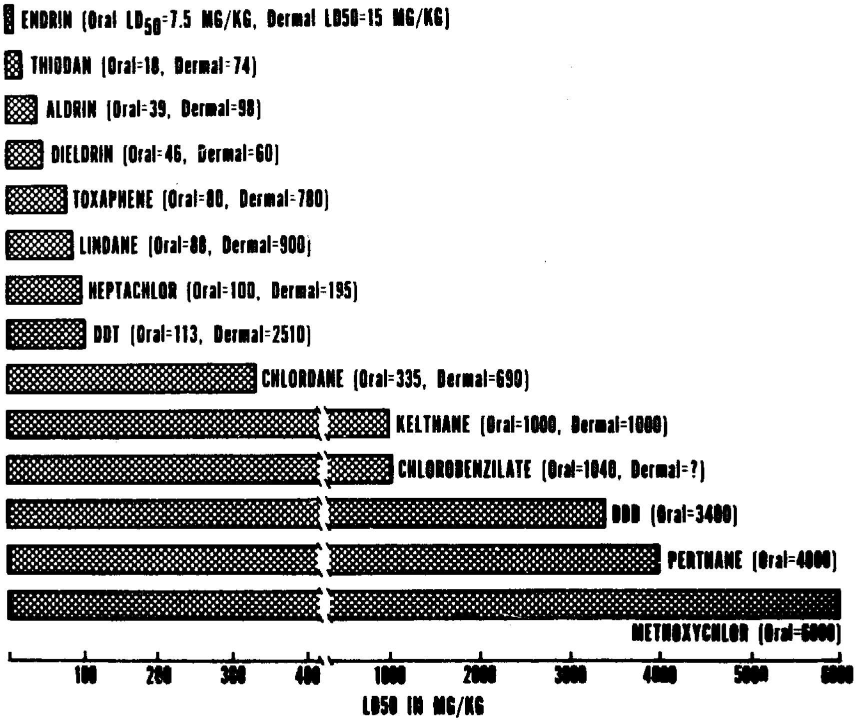

Figure 6-2. *Acute Oral and Dermal Toxicity Values for Some Organochlorine Pesticides*
(Prepared by the Bureau of Occupational Health, State of California Department of Health. Copied with Permission.)

Route of Exposure

Route of exposure is an important determinant of pesticide hazard. Ingestion, inhalation and dermal contact constitute the primary means of pesticide entry. In general, toxic effects are seen most rapidly after ingestion, most slowly after dermal exposure and at an intermediary rate after inhalation.

Ingestion may occur through direct intake when pesticides are improperly labeled and/or stored in containers usually used for potable material (e.g. pop bottles). More commonly, however, ingestion is a result of hand contamination followed by eating or smoking.

Water solubility is an important factor in determining the severity of inhalation exposure. Because the mucous membranes lining the upper respiratory tract hold significant amounts of water, highly soluble vapors will be readily dissolved. This often produces upper respiratory irritation, but also reduces the amount of toxic substance reaching the lungs. Another important factor in determining inhalation exposure is particle size. Aerosol particles of less than one micron can reach the alveoli, while pesticides between one and five microns often reach the bronchial tubes. Particles larger than 10 microns are generally trapped in the nasal cavity or the pharynx (Merkle, C.R.E., 1972).

With respect to dermal exposure, systemic absorption into the blood is enhanced when the skin is inflamed or abraided. In this connection, it is also important that some pesticides may themselves cause skin irritation. This may help to explain why, despite a relatively slow rate of absorption by the skin, this is the most common route for occupational illness. Aside from the question of dermal integrity, some dermal areas tend to absorb pesticides more readily than others. The range is from as little as 12% on the hands to as much as 50% absorption on the face and nearly 100% on the scrotum (Wolfe, 1972).

Duration of Exposure:

Very grossly, toxic responses to chemicals are categorized as acute, subacute, or chronic. Acute effects include rapid onset of serious illness and possibly death. The sub-acute effects produce less serious immediate problems, but may lead to severe illness if the exposure is continued. Chronic effects are those arising from exposure over long periods of time or exposure to a chemical whose effects are not immediately apparent. Chronic effects include such things as carcinogenesis, mutagenesis, and teratogenesis.

MODES OF ACTION OF TOXICOLOGICALLY IMPORTANT TYPES OF PESTICIDES

Although 4,600 companies in the United states produce an estimated 35,000 to 50,000 different pesticide products, only about 100 chemicals can be considered to be widely used as insecticides, herbicides or fungicides. The three chemical groups that at present constitute the greatest public health problems are organophosphates, carbamates and the organochlorine pesticides. The first two groups produce their effects through inhibiting cholinesterase, which is a neurohumoral transmitter in the nervous system. Of these two, the organophosphates are generally more toxic than the carbamates, but both have a short action; in contrast, the organochlorines are more persistent, generally less toxic and are soluble in fat.

Organophosphates. These pesticides combine with cholinesterase at nerve endings in the brain and in the tissues of the body, thereby permitting the accumulation of acetylcholine. The occurrence of symptoms is primarily dependent upon the rate of cholinesterase decline. Symptoms which follow are both muscarinic and nicotinic. Muscarinic effects include nausea, vomiting, involuntary defecation and urination, diarrhea, sweating and blurring of vision. Nicotinic effects includes weakness, fasciculations and flaccid paralysis. When the muscles of respiration are paralyzed, death occurs. Respiratory failure can also occur as a result of blockage of the small bronchi by frothy exudations or by direct depression of the respiratory center. The pharmacological principles involved in therapy are concerned with blocking the effects of acetylcholine on a neuro-muscular system with atropine and by the use of oximes (Davies, 1977; Morgan, 1981). Laboratory confirmation of this illness is achieved by quantitating the amount of cholinesterase in the red blood cell and in the serum. After organophosphate intoxication the red blood cell and plasma cholinesterase recovery occurs at the approximate rate of 1/2 to 4% per day respectively.

Carbamates. These are another group of insecticides whose toxic properties are the result of their cholinesterase inhibition. The signs and symptoms are similar to those seen in organophosphate exposure.

Organochlorines. These are fat-soluble and persistent. There is a wide range of toxicities in this group of pesticides, and endrin has proved to be the pesticide most responsible for episodes of human poisoning. Acute toxic effects are the result of interference with neural axonic transmission, particularly in the central nervous system. Occupational exposure has been shown to produce liver microsomal enzyme induction.

Bipyridyls. Insofar as human toxicity is concerned, paraquat and diquat are the two bipyridyl herbicides which are of special importance. Both are widely used in agriculture for weed control and defoliation. Their toxicity seems to be related to an ability to generate free radicals under occupational exposure. Paraquat is more toxic than diquat and produces proliferative changes in the lung, cornea, optic lens, nasal mucosa, skin and fingernails. Diquat affects the optic lens and gastrointestinal mucosa and fingernails but does not affect the lungs. If ingested, paraquat produces systemic intoxication due to its effects on mucous membrane of the mouth and throat and later as a result of its action on the renal and hepatic systems and fibroblaastic changes in the lungs.

Nitrophenolic Herbicides and Pentachlorophenol. These agents primarily affect the liver, kidney and nervous system. The basic toxic mechanism is the stimulation of the oxidative mitochondrial metabolism by interference with the normal coupling of carbohydrate oxidation in phosphorylation reactions. This leads to hyperpyrexia, tachycardia and dehydration. Most severe poisoning occurs with concurrent high environmental temperature although a major outbreak of pentachlorophenol poisoning occurred in newborns with improperly laundered diapers (Armstrong, 1969). Direct action in the brain may cause cerebral edema, liver parenchyma and renal tubules may show degenerative changes with these agents.

Chlorophenoxy Compounds. These systemic herbicides are locally irritant to skin and mucous membrane. They have a low systemic toxicity but on occasions may exhibit a neurologic effect with peripheral neuropathy.

Dithiocarbamate and Thiocarbamates

Disulfiram inhibits aldehyde dehydrogenase. Such pesticides can therefore induce "Antabuse" reactions in persons who drink beverage alcohols after significant absorption of either dithiocarbamates or thiocarbamates. High levels of acid aldehyde presumably lead to the main pathophysiologic component to these reactions, that is peripheral vasodialation. Shock may occasionally follow and more rarely, circulatory failure.

Fumigants. Fumigants have great power to penetrate the lining membranes of both the respiratory and gastrointestinal systems as well as the skin. They also have the capacity to penetrate some types of rubber and plastic used for protective clothing, and they are not very well taken up by the usual absorbents used in respirators. Butyl rubber should be used for protective clothing. These properties make applicator protection extremely difficult. The chemical mechanisms involved in the toxicity of most fumigants are not well understood.

DBCP (Dibromochloropropane) and EDB (Ethylene Dibromide) are two fumigants which have been widely used as pre-plant fumigants in soil, post-harvest grain fumigants and spot fumigants. DBCP has been cancelled in the United States because it was found to produce sterility in applicators and because it penetrated into the ground water.

EDB, a powerful carcinogenic and mutagenic fumigant with probable adverse male reproductive toxicity, is in addition, very similar chemically to DBCP. Residues have been found recently in flour and bread.

Hydrogen cyanide and its salts poison through inactivation of the cytochrome oxidase of cells in critical tissues, especially the brain and heart. Acrylonitrile degrades slowly to hydrogen cyanide and therefore acts primarily by the same mechanism. However, the slow release of free cyanide from acrylonitrile makes it somewhat less toxic than hydrogen cyanide itself. Both agents are sufficiently absorbable across the skin to produce toxic effects even if inhalation has not occurred. Poisoning manifestations occur mainly because of intracellular anoxia of the central nervous system this produces respiratory failure as well as circulatory failure brought on by myocardial malfunction. The liver has a marked ability to convert cyanide to thiocyanate, a less toxic form. This conversion may be therapeutically accelerated with thiosulfate.

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Chapter 7

First Aid Procedures

Zapatos, C. and Collier, C.

SUMMARY

First aid is the initial effort to assist a victim while medical help is on the way. These procedures when administered as soon as a pesticide poisoning is suspected, may spell out the difference between saving or losing the patient.

PREPARATIONS

Before describing the procedures of first aid management in connection with the use of modern pesticides, it is important to emphasize that wherever pesticides are being stored, handled or used, the following first aid supplies should be on hand:

(1) a supply of water,

(2) a mild soap and rags for washing of the skin, and

(3) home type remedies or antidotes which can be used prior to transporting the victim to a medical facility.

Of the several antidotes which have been recommended for first aid treatment of poisoning, one of the more useful is charcoal. Charcoal is essential for the first aid treatment of pesticide poisonings due to ingestion and should be available for prompt use. When administered in an adequate dose, this adsorbent inhibits gastrointestinal absorption of a broad spectrum of chemical compounds. <u>Activated charcoal</u>, an odorless, tasteless fine black powder, is the residue from the destructive distillation of various organic materials e.g. wood pulp, suitably treated to increase its adsorptive power (Hayes, 1970). A pharmaceutical grade of activated charcoal can usually be purchased at any pharmacy. However, when there is no available pharmacy, an acceptable grade of <u>ordinary charcoal</u> which can be used for treating poisoning cases can be made at home. One common practice is to burn bread crumbs by heating in a semi-closed container until thoroughly charred. An equally good, perhaps better, grade of ordinary charcoal can be made by heating hard wood chips in a closed container so as to exclude air in the actual burning process. The wood should be shaved or cut into small chips and be heated until it is charred black all the way through. A particle may be tested from time to time by breaking it to determine whether it has become completely blackened. The heating should continue with air excluded as much as possible until no more smoke is given off by the homemade charcoal. This may then be powdered or crumbled up by hand and stored in a bottle for use in case of poisoning (Freed, 1981).

Activated charcoal alone is superior to the <u>universal antidote</u> (2 parts activated charcoal, 1 part magnesium oxide and 1 part tannic acid) or the homemade equivalent (2 parts burnt toast, 1 part milk of magnesia and 1 part tea) and should always be used. Another preparation that should be kept on hand is <u>syrup of ipecac</u>, for use to induce vomiting in cases of swallowed poisons. The dose of this is 2 tablespoons for adults and 1 tablespoon for children. NOTE: <u>SYRUP</u> of ipecac <u>NOT</u> fluid extract!

PROCEDURES IN THE EVENT OF A PESTICIDE POISONING

The first step you should take in any poisoning emergency, except when you are alone with the victim, is to call for a physican and/or an ambulance or any vehicle which can transport the victim to the nearest hospital or clinic. If you are alone with the victim, see to it that he is breathing regularly, has an adequate pulse and that no further exposure occurs.

While waiting for the physician or vehicle to arrive, or even while the victim is being transported to the hospital, these first aid procedures should be followed:

Swallowed Pesticides

Steps:

1. If the pesticide is not known, give any of the following adsorbent agents by mouth.

   Activated Charcoal - preferred for all poisons except cyanide and bipyridyls. Dose: 30 gms in 100 ml water (3 tablespoons in 1/2 glass water) as a thick suspension, or

   If activated charcoal is not available, give beaten egg whites. Dose: 8 eggs for adults: 4 eggs for children.

   In case of paraquat an adsorbent clay such as Fuller's earth is preferable to activated carbon. A proprietary clay suspension, Kaopectate® is available from pharmacies in many countries and may be used if Fuller's earth is not available. If none of these clays are available, then uncontaminated earth should be given. From 8 - 10 ounces Fuller's earth should be administered allowing as much time as necessary for the material to be accommodated without distension of the stomach (Collier, 1981).

   Then, bring the victim to the hospital.

2. If the pesticide is known, induce vomiting if recommended on the label and if there are no contraindications.

   After vomiting, give activated charcoal in 100 ml of water (3 tablespoons in 1/2 glass of water) or beaten egg whites if there is no charcoal.

   Bring the victim to the hospital.

Induction of Vomiting

If the identity of the pesticide is known, induce vomiting if recommended on the label. Either syrup of ipecac or gagging are methods used to promote vomiting.

* Syrup of Ipecac -- given by mouth can remove 90-100% of the stomach contents.

* Dose: 2 tablespoons for adults: 1 tablespoon for children.

NOTE: Syrup of ipecac not fluid extract!

Figure 7-1. *Gagging reflex.*

- Gagging -- mechanical stimulation of the throat using the index finger to gag. It is advisable to use the first two fingers of the other hand to force the patient's cheek between his teeth to ensure that he does not bite the index finger. See Figure 7-1. This procedure can remove 50% of the stomach contents and can be done at once. As soon as vomiting occurs, or if it does not occur within a few minutes, give the victim activated charcoal.

Procedures To Avoid In Cases Where Pesticides Are Swallowed

1. Contraindications to induction of vomiting -- do not induce vomiting if the victim:

    - is drowsy, unconscious or in convulsion -- the patient could choke to death if vomiting is induced.

    - has swallowed a corrosive poison because the chemical will burn the throat and mouth as severely coming up as it did going down. Examples are strong acids or alkalis such as phenols and alkaline salts. The victim will complain of severe pain and have signs and symptoms of mouth and throat burns.

    - has swallowed a petroleum based pesticide. Most pesticides that come in liquid formulations are dissolved in petroleum products (xylene, kerosene, etc.). The words "emulsifiable concentrate" or "EC" and "solution" or "S" on the pesticide labels are signals not to induce vomiting if the poison victim has swallowed the concentrate. If the victim has swallowed a diluted form of these products, however, he should be forced to vomit immediately.

    - is in her last three months of pregnancy.

2. The use of table salt (NaCl) to induce vomiting should be discouraged because serious salt poisoning may occur in unsuccessful attempts to induce vomiting (Gleason et al., 1976).

3. No more than two doses of syrup of ipecac should be administered because this drug is injurious to the heart. The fluid extract of ipecac should never be used to induce vomiting because this is fourteen (14) times more concentrated than the syrup (Arena, 1978).

4. Do not give baking soda, sodium bicarbonate and other carbonates in cases of swallowed acidic pesticides, because this may induce perforation of the intestines through the sudden release of carbon dioxide.

Inhaled Pesticides

Steps:

1. If the victim is in an enclosed space, do not go in after him without a respirator.

2. Carry the patient (do not let him walk) to fresh air immediately.

3. Open all doors and windows.

4. Loosen all tight clothing.

Pesticide on the skin

The faster the pesticide is washed off the victim, the less injury will result.

Steps:

1. Remove contaminated clothing.

2. Drench skin with water (shower, hose, faucet, pond, irrigation canal, etc.)

3. Cleanse skin, hair and fingernails thoroughly with plain soap and water. Detergents and commercial cleansers may enhance the absorption of the pesticide through the skin. Avoid harsh scrubbing as this procedure also enhances the absorption of the pesticide (Maramba, 1980).

4. If water and soap are not immediately available, use a dry cloth to blot as much pesticide as possible off the skin and wash as soon as possible.

5. For chemical burns, immediately cover loosely with a clean, soft cloth after washing with large quantities of running water.

6. Avoid using ointments, greases, oils, powders and other drugs in the first aid treatment of burns.

Pesticide in the eye

Steps:

1. Hold eyelids open and wash the eye with a gentle stream of clean running water immediately.

2. Be careful not to contaminate the other eye if only one eye is involved.

3. Continue washing for 15 minutes.

4. Do not use chemicals or drugs in wash water because these may increase the extent of the eye injury.

5. Evert first the upper and then the lower lid and cleanse them with a moist cotton tip to remove any debris.

6. Irrigate the eye once more.

7. Cover the eye with a clean piece of cloth and refer to a physician, preferably an ophthalmologist.

Other first aid procedures:

1. Airway Clearance and Positioning -- it is always imperative to assure a clear airway by removing any foreign body, like dentures, food and secretions from the mouth and by placing the victim in a left lateral Trendelenburg position with head extended and lower than the trunk level by 15 - 30 degrees. See Figure 7-2.

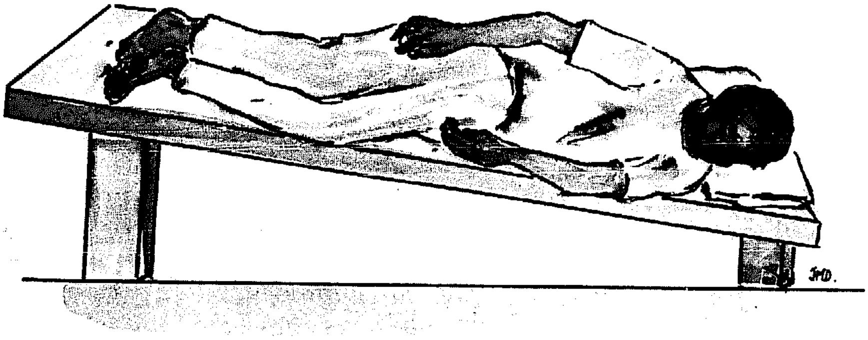

Figure 7-2.
Trendelenburg position.

Maintain this position while waiting for the physician or the vehicle to arrive and while the victim is being transported to the hospital.

This position:

* prevents airway obstruction due to the relaxation of the tongue and other soft tissues. If the tongue has already slipped into the throat, it must be pulled forward.

* prevents the aspiration of vomited material into the respiratory tract.

* enhances the gravity drainage of respiratory tract secretions.

* prevents the further transit of stomach contents into the small intestines where greater absorption of the pesticide can occur in cases of swallowed poisons.

2. Bring the patient to the clinic or hospital.

"DON'T WASTE TIME, GET MOVING."

3. Maintenance of Respiration -- If breathing movements are inadequate or absent, apply artifical respiration using an "ambu" bag or the mouth-to-mouth resuscitation.

4. Maintenance of Circulation -- When pulses suddenly disappear and there are no detectable heart sounds, apply external heart massage. See Figure 7-3.

Figure 7-3. *Cardiopulmonary Resuscitation*

5. Unconsciousness -- Never give anything by mouth and make sure that the tongue is held forward by inserting a small hard blunt object such as a spoon or a tongue depressor between the tongue and roof of the mouth.

6. Convulsions -- Insert a padded gag between the jaws to prevent victim from biting his tongue. Prevent additional injury by placing a pillow or cushion under his head and preventing him from falling.

7. Prophylaxis and First Aid Antidotal Medication -- Atropine sulfate and oximes should not be taken by pesticide users as a prophylactic measure because they do not prevent poisoning. In fact, they can create a false sense of security and delay the administration of first aid procedures and definitive medical treatment. Atropine sulfate tablets can mask or delay early symptoms of poisoning and this can be detrimental in at least two ways. Workers can go back to work and get more exposure or, if the worker is taken to a physician who has not been informed that atropine has been taken, the diagnosis of poisoning can be missed or delayed. In an acute poisoning emergency, do not use oral atropine as a first aid measure because the dose is too small and the victim cannot take medicines by mouth if he is vomiting or stuporous (Anon., 1974).

8. Identification of the Pesticide -- If at all possible, take the pesticide container or label with you to the physician. See Figure 7-4. If this is impossible, make sure you know what pesticides the victim has been using.

Figure 7-4. *Take the bottle or container to the doctor.*

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Chapter 8

Clinical Aspects of Acute Poisoning

A. Acute Systemic Poisoning
B. Topical Effects

Levine, R.S. and Davies, J.E.

SUMMARY

Essentials of diagnosis and management of the more important pesticide poisonings are presented including the organophosphates, the carbamates, the organochlorines, bipyridils, nitrophenolic and chlorophenoxy herbicides.The major topical effects of pesticides on the skin and eyes are also reviewed.

INTRODUCTION

Clinical management of adverse pesticidal effects became a major subject for medical concern after World War II. One important group of chemicals, the organophosphate insecticides, had been developed as a war gas, and another major group, the organochlorines, had been developed and used to control malaria and typhus, both of which were epidemic during this period.

Since then, thousands of pesticide combinations have been introduced into man's environment, and more than 80 are known to have produced illness. Today's physician has acquired at least three new medical responsibilities as a result of the introduction of this technology: (1) management of a wide variety of pesticide intoxications; (2) implementation of schemes for pesticide worker protection; and (3) advising the general public on the problems and hazards of human pesticide pollution.

ACUTE SYSTEMIC POISONING

Organophosphates and Carbamates Insecticides (Cholinergic Illness)

Organophosphate and carbamate insecticides represent the chemical groups which cause most acute systemic poisonings. Ultimate recovery depends very much upon early diagnosis and vigorous treatment.

Symptoms and Signs

Symptoms and signs of systemic organophosphate and carbamate poisonings are almost entirely due to cholinergic manifestations. They include both muscarinic and nicotinic effects and are the result of acetylcholine accumulation. Early symptoms depend on the route absorption and the severity of the intoxication.

Muscarinic effects, usually precede nicotinic effects, but these two may coincide if the dose is high.

Muscarinic effects include:

- anorexia
- nausea
- vomiting
- diarrhea
- involuntary defecation and urination
- sweating
- salivation
- lacrimation
- pain in the chest
- excessive bronchial secretions
- blurring of vision due to miosis.

* * *

Nicotinic effects include:

- muscle twitching
- fasciculations
- weakness
- flaccid paralysis.

With involvement of the muscles of respiration, respiratory failure may occur from bronchial constriction and blockage by secretions. Ultimately the respiratory center itself may be affected.

Central nervous signs and symptoms include anxiety, restlessness, lightheadedness, headache, drowsiness, convulsions and coma.

In severe cases, the patient is pale, sweating and frothing at the mouth. The pupils, usually miotic and non-responsive to light, may be dilated if the patient is in extremis. In the latter case, they will become miotic with treatment.

The most important neurological findings are:

- Localized and generalized involuntary twitching which may be elicited by tapping the muscles over the cheekbone, over the thorax, or on the arms. Generalized clonic seizures may occur.

- Miosis--the pupil will be small and the diameter of the pupils in millimeters should be recorded.

Additional signs and symptoms include the following:

- Elevation of the blood sugar may be noted, and glycosuria detected. The level of hyperglycemia is less than is observed with diabetic coma,and ketoacidosis is rarely seen. The serum electrolytes are usually normal, though hypokalemia may occur and be aggravated by diuretic therapy. Serum potassium levels should be checked early. Fever is not a constant finding; in fact the patient's temperature is usually normal or subnormal unless severe dehydration coexists. A polymorphonuclear leukocytosis is a common finding.

Acute poisoning usually manifests itself quite rapidly. Occasionally, however, there may be a delay of up to 12 hours especially following poisoning by a fat soluble organophosphate insecticide such as dichlofenthion (Davies, et al., 1975). The sequence of signs and symptoms may be influenced in part, by the route of absorption. After inhalation, respiratory effects may be the first to appear, while after ingestion, gastrointestinal problems are dominant. In children, a convulsion may be the first sign.

The symptoms and signs of <u>mild</u> poisoning include headache, fatigue, dizziness, blurred vision, excessive sweating, nausea and vomiting, abdominal cramps, salivation and miosis. <u>Moderately severe</u> poisoning may cause all of the aforementioned symptoms and in addition, may produce chest discomfort and tightness, marked miosis, slow heart rate, muscular twitching, confusion, ataxia, slurred speech and occasionally toxic psychosis with manic or other bizarre behaviors. <u>Severe</u> poisoning may have many manifestations including loss of deep tendon reflexes, local or generalized seizures, fecal and/or urinary incontinence, shock and cardiac rhythm irregularities (including complete heart block), but the most critical problem is that of impaired pulmonary function. Progression from mild and moderate signs and symptoms to severe illness is unpredictable and may be very rapid; death is due to respiratory failure.

Organophosphate Insecticides (e.g. Azinphosmethyl)

Case Presentation

A review of the clinical features of organophosphate poisoning is illustrated by the following:

> *The patient was a 34 y/o 70 kg black male who had accidentally ingested approximately 3 ounces of azinphos-methyl (0,0-dimethyl S-(4-oxo-1,2,3-benzotriazine-3(4-H)-yl-methyl phosphorothioate oral LD 50 13.0-16.4 mg/kg).*
>
> *Somebody had placed the pesticide in a Coke bottle in the kitchen which he accidentally ingested. When seen in the emergency room 30 minutes later, he was confused, had vomited and his pupils were widely dilated. The admission red blood cell cholinesterase was 0.12 ΔpH/hr and the plasma was 0.17ΔpH/hr (Michel method). In spite of receiving 13 mg of atropine I.V. and 1 gram of 2 PAM I.V. over one hour, his condition deteriorated although his pupils had now become miotic.*

Forty-eight bottles of atropine and 9 bottles of 2-PAM were required to treat this patient.

> *His condition remained severe for the next five days during which time he received 383 mg of atropine I.V. and 9 gram of 2-PAM. It was not until 171 mg of atropine were given in a single 24-hour period that a pupillary response was finally noted and he began to improve. The daily therapy and the concomitant enzymatic changes during the five days of management of this case are shown in Figure 8-1.*
>
> *Initially the pupils were dilated, but then became constricted and remained so for 5 days until, eventually, atropine toxicity resulted in further dilation of the pupils. The admission findings may be confusing unless it is remembered that pupillary dilation rather than miosis have been noted in 13% of cases when first seen. The lesson was the need to titrate atropine dosage against pupillary response rather*

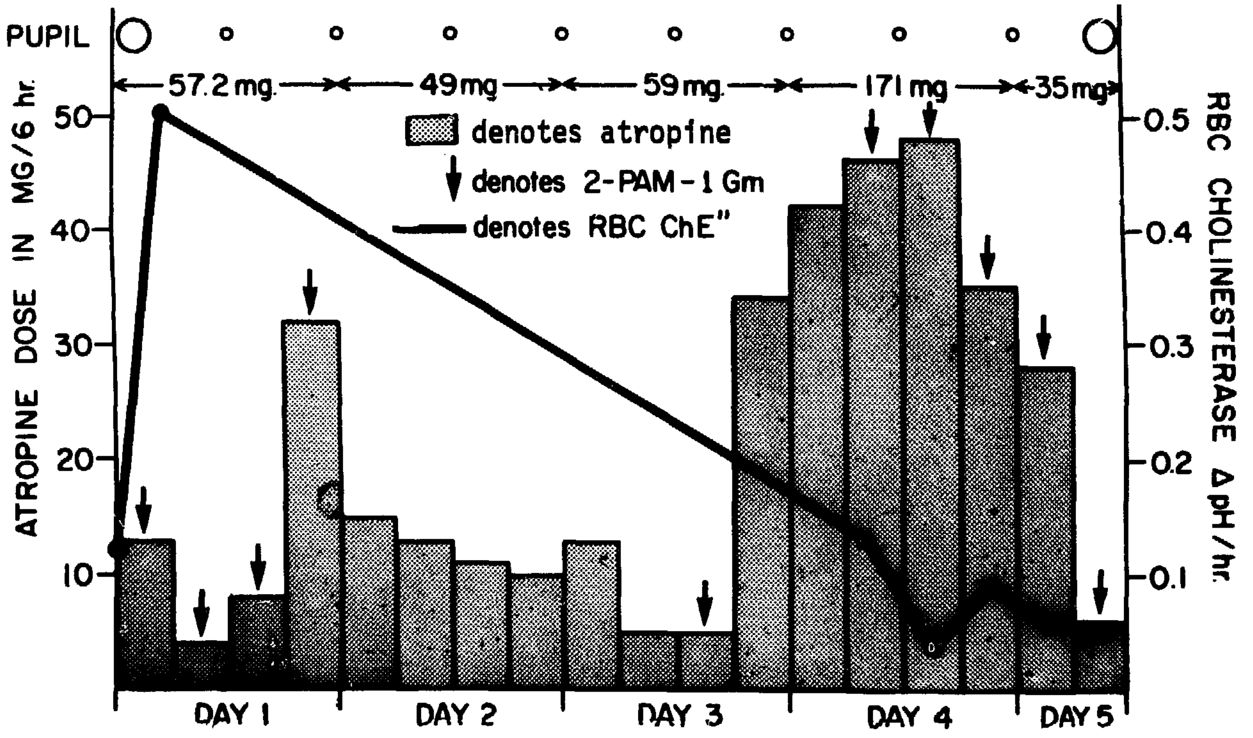


Figure 8-1. *Clinical and therapeutic response of azinphos-methyl poisoning.*

than cholinesterase levels. The arrows denote when 2-PAM was administered, and the reactivation of the red blood cell cholinesterase can be noted following the administration of 2-PAM on the first day; subsequent to this, "aging" occurred and the later administration of 2-PAM produced no release of free red blood cell cholinesterase.

Diagnostic Features

Initial diagnosis and institution of appropriate treatment of suspect cases must be made on clinical grounds alone for these organophosphate and carbamate insecticides. In severe poisoning cases, there is not enough time to wait for confirmatory laboratory results.

The most important factors in the clinical diagnosis of organophosphate and carbamate poisoning are a positive pesticide exposure history, the symptoms and signs typical of anticholinesterase illness, and the presence of atropine refractoriness.

The rapidity with which symptoms appear may aid in obtaining the pesticide exposure history, particularly after ingestion and inhalation. With few exceptions, the patient will begin to feel ill within 15 minutes to an hour after ingestion although delays of 4 to 12 hours may occur. It is important to remember that there may not always be an obvious exposure history. Problems may arise in the case of a small child who has been in the fields. There should be specific inquiry as to the history of geophagia, since the possibility of exposure by this route may not be realized. With respect to dermal exposure, the patient may not mention that his or her shirt, pants or shoes were wet from the pesticide or from moist residue on leaves. In arid areas, dermal exposure occurs from dry, dusty residues on the leaves of plants and there may be no sensation of wetness. With respect to symptoms and signs, these may be confused with those of other conditions. Miosis, however, is a rare condition in many clinic settings and should always lead to the consideration of exposure to organophospate or other anticholinesterase pesticides. Miosis is particularly significant if accompanied by other signs of cholinergic illness. Finally, it may be useful to observe the effect of atropine. Patients with organophosphate or carbamate poisoning are resistant to the reactions of atropine, and failure of one to two milligrams administered parenterally to produce signs of atropinization (flushing, tearing, rapid heart rate and dryness of the mouth) is strongly suggestive of toxic cholinergic illness.

There are subtle and important clinical differences between organophosphate and carbamate insecticides. Most differences are due to the fact that cholinesterase reactivation is much more rapid after carbamate exposure than it is after organophosphate exposure (Vandekar, 1975). The onset of symptoms is usually immediate with carbamate exposure, but it may be delayed for several hours following exposure to organophosphates, especially if the compound has a high octanol partition coefficient. The dose necessary to produce incapacitating symptoms is generally far from the lethal dose for carbamates, while the two doses are often quite close for organophosphates.

Laboratory Verification

Definitive verification of organophosphate poisoning calls for quantitative measures of cholinesterase activity. Cholinergic quantitation is essential for verification since cholinergic illness can mimic a variety of more common conditions.

Two types of circulating cholinesterase are frequently measured. These include "pseudo" cholinesterase which is found in the plasma, the liver and the nervous system and true acetyl cholinesterase, which is found in the nervous system and the red blood cell. The action of both types of cholinesterase is inhibited by the organophosphates, but red blood cell depression is a better clinical indicator of potential adverse neurological effects. It is important to note that reactivation of red cell cholinesterase will occur after the administration of Pralidoxime if the oxime is given early. In this instance, the patient may have normal red blood cell levels due to oxime reactivation, even while exhibiting cholinergic manifestations. With some organophosphates, "aging" occurs early and oxime therapy fails to reactivate cholinesterase (Hobbiger, 1963). In cases of carbamate poisoning, cholinesterase reactivation may occur in the test tube used for blood collection; again, a discrepancy may be evident between the normal laboratory values and the patient's abnormal clinical conditions.

With respect to plasma cholinesterase, low levels may be found in certain disease states: malnutrition, fever, myocardial infarction, disseminated sclerosis, and liver disease; after certain drugs and toxicants such as carbon disulphide and organic mercury compounds which may impair the synthesis of the enzyme by the liver; and a result of genetically determined low plasma cholinesterase. This last condition may also lead to respiratory arrest after being anesthetized with succinylcholine, a defect which occurs in 3% of the population. Low red blood cell cholinesterase may also be found in conditions which impair red blood cell integrity, such as paroxysmal hemoglobinuria or in a newborn after a complicated delivery (Kalow, et al., 1956).

With respect to urinary metabolite studies, breakdown products of pesticide in urine are excellent indices of exposure to organophosphates and carbamates, and their concentrations in urine can be used as a measure of the severity of the poisoning and its probable duration; they are discussed in more detail in Chapter 10.

The identification of intact pesticides in the blood or gastric contents is a third way the laboratory can confirm cholinergic illness.

The methods of collecting specimens and the different cholinesterase and urinary metabolite data are discussed in Chapters 9 and 10.

Treatment

Treatment of acute cholinergic illness depends on the severity of exposure. In very mild cases, simple removal from exposure may be all that is required. In severe cases, however, a more vigorous approach is needed. The speed required in a serious intoxication, particularly with a child, is similar to that required by a patient with ventricular fibrillation or cardiac arrest.

In serious cases with compromised respiration, the first priorities are:

- Airway clearance and oxygenation.
- Removal of dentures and clearance of mucous and debris from the mouth and pharynx, preferably using suction.
- Introduction of an oro-pharyngeal or naso-pharyngeal airway and administration of oxygen by mask or via the nasal route.
- Serial blood gases should be drawn to monitor respiratory and metabolic progress.

When cyanosis is overcome, specific antidotal therapy with atropine should be started. (It is important to note that atropine may induce a ventricular fibrillation in the presence of cyanosis). Ideally, atropine should be given intravenously, but if this is not possible, the intramuscular route will suffice. The dose of atropine for adults including children over 12 years of age, is 0.4 to 2.0 mg (1.0 to 5.0 cc of the usual 0.4 mg per cc solution) repeated at 15 to 30 minute intervals until atropinization is achieved. For children under the age of 12, the dose is 0.05 mg per kg of body weight (0.125 cc per kg of the usual 0.4 mg per cc solution), again repeated every 15 to 30 minutes until the achievement of atropinization. Signs of atropinization include dry, flushed skin, tachycardia and pupil dilation. A mild degree of atropinization should be maintained for at least 48 hours. In cases of severe poisoning, the patient will show atropine tolerance and an increase (even doubling) of the doses previously suggested may be required.

Pralidoxime (2-PAM, Protopam) chloride is a cholinesterase reactivator which provides an important adjunct to atropinization when administered soon after the poisoning contact in cases of organophosphate poisoning. On the other hand, Pralidoxime is contra-indicated in cases of carbamate poisoning (Hayes, 1967). Specifically, Pralidoxime is important in combating the nicotinic effects of organosphosphate poisoning as manifested by muscle weakness and twitching, and most particularly by dyspnea. For patients over the age of 12 years, 1.0 gram is given intravenously, no faster than 0.5 grams per minute, with the dose being repeated in one hour if signs of nicotinic toxicity have not been relieved. For children of 12 years and under, 20 to 40 mg/kg is given intravenously depending on the severity of the poisoning. No more than half of the total dose is injected per minute. The dose can be repeated every 10 to 12 hours as indicated, up to three times. Slow, continuous administration may be accomplished by giving Pralidoxime over a 30 to 60 minute interval in 250 cc of normal saline. If intravenous administration is impossible, deep muscular injection of Pralidoxime may be used. It is important to note that Pralidoxime may cause respiratory depression, and the physician must be prepared to assist pulmonary ventilation if this occurs.

Once the patient has been stabilized with respect to provision of an adequate airway and administration of specific antidotal therapy, decontamination should be started. Persons attending the patient should avoid direct contact with contaminated clothing or vomitus. The attendant should put on rubber gloves, undress the patient and place all clothing in a plastic bag which is carefully labelled. The patient must be thoroughly bathed with large amounts of soap and water. It is also important to rinse the hair thoroughly and to remove any residue from under the nails.

Decontamination also includes the removal of the ingested pesticide by the induction of vomiting, gastric lavage and the limitation of gastrointestinal absorption as appropriate.

In addition to specific antidotal therapy, supportive therapy may be required for convulsions. It is important to consider the possibility that conditions unrelated to pesticide toxicity are responsible including trauma, cerebral anoxia or poisoning from another source. If the convulsions do not respond to the specific antidotal therapy, Diazepam (Valium) given in a dose of 5 to 10 mg for adults (repeated as needed at 10 to 15 minute intervals to a maximum of 30 mg), 0.2 to 0.5 mg for infants over 30 days of age and children under 5 years (repeated as needed every 2 to 5 minutes up to a maximum of 5 mg) and for children 5 years of age or older, 1 mg (repeated as needed every 2 to 5 minutes to a maximum of 10 mg) is probably the most reliable therapy. The intravenous route rather than the intramuscular route is preferred. The drug should be given slowly via a large vein with no more than half the total dose per minute. The physician must be prepared to assist pulmonary ventilation mechanically in the event of respiratory depression and to counteract sudden hypotension. Extreme caution is needed if the patient has chronic lung disease or unstable cardiovascular status.

Since respiratory embarrassment, should it occur, is usually secondary to increased bronchial secretion rather than pulmonary edema, aminophyline, reserpine, phenothiazine tranquilizers, succinylcholine, furosemide and other such agents are generally contra-indicated in organosphosphate poisoning.

The patient should be closely monitored for at least 24 hours after returning to normal because very serious relapses may occur due to continued absorption of the poison or the wearing off of antidotal effects.

A patient who has recovered after acute poisoning remains very susceptible to any anticholinesterase agent for several weeks. Regeneration of cholinesterase occurs mainly through new enzyme synthesis and proceeds at about 1% per day. If pre-exposure levels are available, the patient should not be re-exposed to cholinesterase inhibitors until blood cholinesterase activity has been returned to at least 80% of these values and all signs and symptoms of poisoning have completely resolved.

Organochlorine Insecticides

These insecticides, though less widely used because of increased insect resistance, are still very important from a clinical point of view because the organochlorines:

(1) still cause systemic poisonings from time to time;

(2) are fat-soluble and important members of the pesticide residue body burden in most parts of the world;

(3) are powerful liver microsomal enzyme inducers; and

(4) are highly persistent in the environment and have the potential for deleterious impact on non-target species.

Symptoms and Signs

Initial signs and symptoms depend, in part, upon the route of exposure. Nausea and vomiting often occur soon after ingestion. This is followed by apprehension and excitability, and then by various neurologic signs including twitching, tremors, mental disorientation, weakness, parasthesiae, and convulsions which are often epileptiform. Respiratory depression may be caused by both the pesticide and its petroleum solvents. Headache and dizziness have also been reported. Pallor occurs with moderate to severe poisoning though cyanosis may occur if respiration is impaired.

Case Presentation

A 2-year-old boy was brought to the emergency room of a local hospital. On arrival he had a convulsive seizure. The parents reported that the child had ingested an unknown amount of an insecticide. The child was hyperactive, ataxic, and unsteady. He fell down when he tried to walk. Pupils were 2 to 3 mm in size. There was no vomiting, sweating, or increased bronchial secretions. The chest was clear. He was given diphenylhydantoin and a large intravenous dose of phenobarbital. He was admitted to the Pediatric Intensive Care Unit for observation. Both heparinized and whole blood were collected. By the Michel method *the RBC cholinesterase was 0.69 ΔpH/hr, and the plasma cholinesterase was 0.90 ΔpH/hr which are normal enzyme levels with this method. Blood tests for intact pesticide, however, identified dieldrin in a concentration of 407 ppb. This confirmed an organochlorine pesticide poisoning due to dieldrin. An important lesson is that acute poisoning may still be caused by organochlorine pesticides in the home even though these pesticides are not commercially available.*

Diagnostic Features

The differential diagnosis includes other toxic causes of convulsions; epilepsy; metabolic disturbances; kidney failure; hypoxia; and infectious diseases.

Laboratory Verification

In case of suspected organochlorine poisoning, 10 cc of blood should be drawn in a plain test tube, the sample labeled and the blood allowed to clot. The serum should then be separated and submitted frozen to a definitive chemistry laboratory for appropriate gas chromatography studies. There is considerable individual and chemical variability as to the serum organochlorine level which is associated with convulsions. With regard to dieldrin, for example, it has been noted that seizures do not appear to occur with levels below 200 ppb.

Treatment

The first priority in treatment is to establish a clear airway to maintain oxygenation, if necessary, by assisted pulmonary ventilation with oxygen. Secretions should be aspirated. If poisoning is due to ingestion, the gut should be decontaminated. Bathing and shampooing will decontaminate skin and hair. For convulsion control, the drug of choice is Diazepam (Valium®). The second choice for treatment of convulsions are the barbiturates. Pentobarbital (Nembutal®) has been used successfully in the past. Another drug which may be used is phenytoin (Dilantin®) which has an added advantage because of its ability to remove organochlorine pesticides stored in the adipose depot. Studies have shown that 80 to 90% of stored DDT and its metabolites as well as dieldrin were eliminated during a period from 30 to 9 months of Dilantin therapy (Davies, et al., 1971).

Herbicides

Bipyridyls

Exposure may occur with this group of chemicals either by inhalation, skin absorption or ingestion; paraquat and diquat are the two most important members of this chemical group. There are no known substantiated cases relating the development of systemic paraquat poisoning following normal agricultural use of the chemical (J. Ford, personal communication, 1982). There are, however, reports of cases in the medical literature involving patients that have developed paraquat poisoning following extensive contact of the chemical with pre-existing dermal abrasion or ulcer (Horiuchi & Ando, 1980).

Symptoms and Signs

Both topical and systemic effects can occur with respect to paraquat; and dermal contact may be followed by skin irritation, drying and cracking. Heavy skin exposure produces damaged fingernails, with a common lesion being transverse bands of discoloration; and other signs include loss of nail surface, transverse ridges, gross deformity of the nail plate and loss of the nail. Paraquat is an irritating chemical if allowed to remain in contact with the skin. Unless paraquat is removed from the skin, prolonged contact with the concentrate or repeated daily contact with the spray dilution may result in a dermal burn or ulceration. In such situations, further exposure to the chemical may result in systemic paraquat poisoning. Painful redness and swelling of the conjunctiva as well as corneal clouding may develop 12-24 hours after paraquat eye contact. Inhalation overexposure to paraquat spray mist may result in the development of nosebleed, sore throat and coughing. However, once exposure has been discontinued these effects remit within a few days.

The clinical picture following accidental or suicidal ingestion of paraquat is very different, and ingestion of paraquat may be fatal; however, if the dose is not overwhelming (<50 ml concentrate) and the recommended treatment is initiated within the first 24 hours, the patient's prognosis is favorable.

Three clinical stages may follow ingestion of as little as an ounce of paraquat. The first is a gastrointestinal phase with burning of the mouth, throat, and nausea soon after exposure. Vomiting is a common occurrence. Next signs of hepatic and renal toxicity appear. These are due to central zone necrosis of the liver and acute tubular necrosis of the kidney. Liver and kidney damage are usually reversible, however. Seventy-two to 96 hours after ingestion, cough, dyspnea and tachypnea signal that pulmonary damage has occurred. These signs and symptoms may be delayed up to twenty hours after ingestion. Hyperplastic changes in the terminal bronchioles occur with alveolar fibroblastic proliferation. Death may occur with a few days from respiratory failure although in a few cases, paraquat ingestion has been associated with pulmonary edema which resolves within a few days without serious permanent damage.

In contrast with illness following small doses of paraquat, ingestion of 100 mil or more of the concentrate is usually associated with a dramatic gastrointestinal phase involving the loss of the digestive tract mucosa and massive pulmonary edema. Typically these individuals die within 24-48 hours regardless of the type of treatment administered.

Diquat ingestion results in nausea, vomiting and diarrhea with accompany-dehydration. Melena and hematemesis result from gastrointestinal ulceration. Diquat appears to be more toxic to the kidneys than paraquat, and onset of coma may be rapid, possibly as a result of electrolyte disturbances or central nervous system hemorrhage. Unlike paraquat, it is not actively accumulated by the lung and does not produce the characteristic paraquat poisoning syndrome. However, ingestion of large amounts of diquat (>50 ml of concentrate) will result in massive pulmonary edema.

Case Presentation Paraquat

A thirty-six year old male with suicidal intent, ingested approximately two ounces of paraquat concentrate. He vomited several times and was hospitalized approximately eight hours later. Emergency room treatment consisted of further induction of emesis and administration of repeated suspensions of activated charcoal. The initial (eight hour) analysis of the patient's urine and blood for paraquat revealed the presence of 120 and 0.178 parts per million (ppm) paraquat respectively.

The patient was administered the recommended treatment for paraquat poisoning. This procedure included giving repeated suspensions of Bentonite clay and a magnesium cathartic every four to six hours, forced diuresis (14 to 16 liters per day), hemoperfusion and hemodialysis and adminstration of a low concentration of inspired oxygen.

Approximately thirteen hours after ingestion the paraquat urine and blood levels were reduced to 2.9 and 0.36 ppm respectively. The initial hemoperfusion resulted in a drop in platelets which necessitated its discontinuation and the patient was then placed on hemodialysis. Paraquat blood levels at 24-hours demonstrated a reduction of the chemical to 0.14 ppm. This was compatible with comparable paraquat blood levels found in previous patients who had survived paraquat poisoning.

On day two, examination of the digestive tract revealed extensive esophagitis and gastritis with some ulceration and blood observed in the stomach. There was no evidence of irritation or ulceration of the duodenum. BUN and creatinine levels were normal and the chest X-rays appeared clear at this time. The patient's platelet count recovered sufficiently so that hemoperfusion could be continued, thus further reducing the arterial blood paraquat levels to 0.01 to 0.07 ppm. Several hours later there was a drop in the platelet count thus requiring the discontinuation of hemoperfusion and placing the patient on hemodialysis.

On day three, the patient demonstrated severe irritation and ulceration of the mouth and pharyngeal areas. There was also infiltrates evidenced by chest X-ray which appeared at the middle and left lung lobes and persisted for six to seven days. During the next ten days the patient became oliguric and the chest X-rays continued to demonstrate signs of progressive infiltration. The administration of the clay suspensions was continued in addition to the alternating use of hemodialysis and hemoperfusion.

By the second week, the patient demonstrated signs of marked improvement. Although paraquat could no longer be detected in the blood, there were still detectable levels found in the patient's urine. Kidney function had returned to normal, the pharyngeal and oral lesions subsided and there was a clearing of the chest X-rays. The other pulmonary parameters e.g. blood gasses and pulmonary function testings were also improving.

At discharge on day twenty-two, moderate pulmonary restriction was indicated by lung volumes in the range of 30 to 40% of that predicted for his size and age. Pulmonary function testing was continued after his discharge. It was not until the second month after ingestion of paraquat that his pulmonary function had returned to normal. Paraquat was detected in the patient's urine until day forty-four (limit of detection 0.007 ppm). The patient has taken up jogging and now runs with no apparent pulmonary handicap.

Diagnostic Features

Clinical diagnosis is based upon a history of exposure followed by typical early symptoms and signs, which must nonetheless be differentiated from other causes of skin irritation, conjunctivitis, corneal clouding, mucous membrane irritation, gastrointestinal distress, etc.

Laboratory Verification

Ideally, analytical techniques capable of detecting concentrations below one part per million should be used. If the physician analyzes the patient's urine or blood by a less sensitive method, then there is a good chance that paraquat will be missed and the patient's condition misdiagnosed. Fortunately, gas chromatography, radioimmune assay, and colorimetric methods with the required sensitivity have all been reported (Proudfoot, et al., 1979). One colorimetric method involves less than 20 minutes of laboratory time (Knepil, 1979).

Recently, plasma concentrations of paraquat were observed in 79 patients who had ingested liquid or granular paraquat. At any given time, the plasma concentrations of paraquat in those patients who died exceeded concentrations in survivors, and early measurement of plasma paraquat was useful in assessing the severity and predicting the outcome of poisoning. Patients whose plasma concentration did not exceed 2.0, 0.6, 0.3, 0.16 and 0.1 mg per liter in 4, 6, 10, 16, and 24 hours respectively, were likely, to survive (Proudfoot, et al., 1979).

In another report, involving two cases, plasma paraquat levels of 1.12 mg per liter 34 hours after ingestion and 1.44 mg per liter 15 hours after ingestion have been described. These two patients were hemoperfused with acrylic hydro-gel coated activated charcoal for an average of 8 hours per day for 2 to 3 weeks. Platelet loss was overcome by platelet concentrate transfusion. Both patients survived. It was concluded that these patients would have died from pulmonary fibrosis due to paraquat accumulation in the lungs but for the successful hemoperfusion regimen, and it is possible that coated activated charcoal had removed paraquat from the blood faster than the rate in which it could accumulate in the lungs (Okonek, et al., 1980).

Treatment

Vigorous therapy involves hemoperfusion with coated activated charcoal as frequently and as soon as possible. Moreover, gastrointestinal decontamination with 8 to 10 ounces of Fuller's Earth suspension (30 mg per 100 cc) should be carried out even if the patient appears well. In any cases of paraquat ingestion, then, it is recommended that the gut be cleaned by induction of emesis or performing gastric lavage. This procedure is followed by administering repeated suspensions of a paraquat binder e.g. Fuller's earth, (30 mg per 100 cc) in addition to a magnesium sulfate cathartic (the suspensions of Fuller's earth should be administered every three to four hours for approximately three days). If Fuller's earth is not available, then administration of suspensions of activated charcoal is recommended. It has been determined *in vitro* that activated charcoal is about 80% as effective in binding paraquat as Fuller's earth (J. Ford, Personal communication, 1982).

The paraquat blood levels can be reduced to minimize pulmonary accumulation of the chemical by means of forced diuresis and hemodialysis and/or hemoperfusion. A target urine volume of 12-14 liters/day has been recommended in conjunction with the extensive utilization of hemodialysis and hemoperfusion. The adequacy of the gut clean-out and the paraquat blood levels will aid the physician in determining the time required to maintain the patient on this treatment regimen.

Regarding pulmonary support, it is important to note that increased alveolar oxygen concentration may accelerate the pathologic processes in the lung caused by paraquat. The patient's clinical condition and the effectiveness of the treatment can be evaluated by monitoring the following: (1) blood gases; (2) BUN and creatinine; (3) liver enzymes; (4) chest X-rays; (5) paraquat analysis, (urine, blood, and dialysate). Concerning external exposure, contaminated skin and eyes should be treated with large amounts of clear water for purposes of decontamination. Mild skin reactions usually respond to removal from further contact with bipyridyl. All eye contact as well as severe skin damage should be treated by referral to specialists in ophthalmology and dermatology respectively. Paraquat is manufactured by Chevron Chemical, whose telephone number is (415) 233-3737 if toxicologic assistance is required.

Nitrophenolic and Phenolic Herbicides (e.g., Dinitrophenol and Pentachlorophenol):

Exposure

These agents primarily poison by inhalation or by dermal absorption although gastrointestinal absorption is rapid when it occurs.

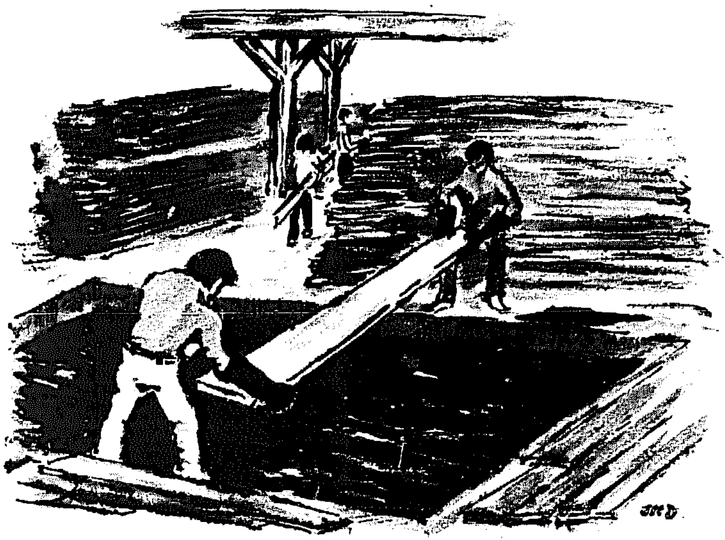
Symptoms and Signs

Both agents exert profound metabolic influence by blocking oxidative phosphorylation. Compensatory metabolic activity of all body cells leads to temperature elevation (up to 110°F) rapid breathing and rapid heart rate. Because respiratory and cardiac stimulation do not accelerate in proportion to the increased metabolism, anoxia and acidosis developed rapidly. Lesser degrees of poisoning may be manifested by sweating, headache, weakness, malaise and nausea. Superficial manifestations of pentachlorophenol poisoning include irritation of the nasal, oral and ocular mucous membrane as well as the skin. Also, nitrophenolic chemicals may cause yellow discoloration of skin and hair.

Case Presentation

During visitr to the Far East, reports of numerous pentachlorophenol poisonings were encountered when this wood preservative was used to prevent Blue Spot fungus infection of timber. The major causes of poisoning could been attributed to climatic factors since many treatment plants were located near or on the Equator, and the work was being done in a very hot and humid environment. Dermal and respiratory routes of absorption were not recognized and timber boards were hand-dipped into large open tanks containing a mixture of sodium pentachlorophenate (4.5%-10%) solution with gamma benzene hexachloride

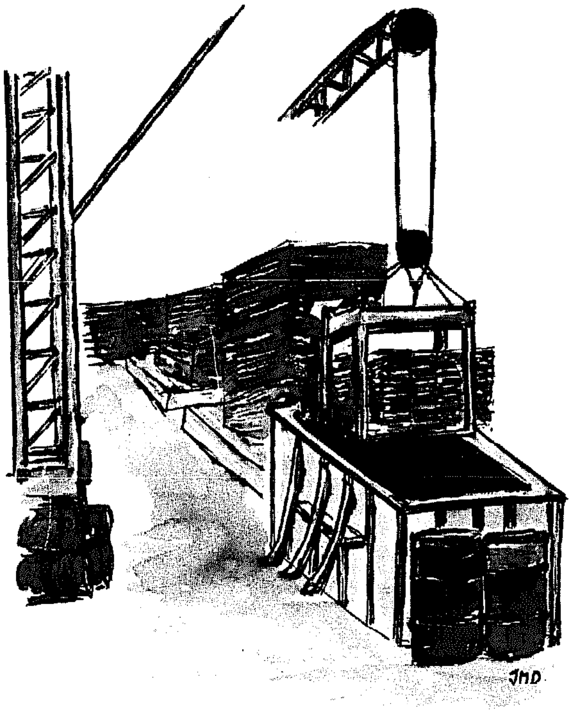
(0.85%) and borax (0.55%). Symptoms and signs were weakness, flushing high fever, pneumonia and dermatitis. Eleven people had died shortly after admission to the hospital. All except one were males (the female with similar clinical features turned out to have drunk some of the pentachlorophenol in an unsuccessful suicide attempt).



Dermal risks from hand-dipping timber into PCP tanks.

In another timber treatment plant, boards were mechanically dipped into a settling tank. Dermal exposure was less in this setting, but respiratory exposures were exacerbated by use of bubbled air to mix the insecticide in the settling tank. The use of conventional protective clothing was casual and incomplete so poisoning became a serious public health problem.

Respiratory exposure resulting from air bubbling through PCP settling tanks.



Diagnostic Features

Diagnosis may be suggested by history of exposure especially to wood preservatives. Poisoning must be differentiated from other causes of mucous membrane irritation, such as infection or allergy. Other causes of elevated temperature should be considered.

Laboratory Verification

Both types of agents can be measured in blood and urine. Treatment should not be delayed pending laboratory confirmation. Also, 84.8% of persons in the United States population have been found to show detectable pentachlorophenol in the urine, and such usual exposure must be differentiated from levels associated with acute intoxication (Kutz, et al., 1978).

Treatment

Skin and hair need to be decontaminated with thorough washing. Attendants should take care to protect themselves from exposure. The eyes should be thoroughly flushed with clean water. Gastrointestinal decontamination is indicated in cases of ingestion. In the event of systemic poisoning, body temperature should be reduced by physical means including sponge baths and low temperature blankets. Fully conscious patients should receive cold, sugar-containing liquids orally ad libitum. Oxygen should be administered continously by mask for anoxia and intravenous fluids given at maximum tolerated rates. Circulating electrolytes and sugar should be monitored. Sedatives can be used if necessary to control apprehension, excitement, and/or convulsions.

Aziaprine, aspirin and other antipyretics should not be used for the high fever. Animal tests have shown that aspirin enhances rather than reduces toxicity with these agents. Additionally, it is important to administer a well-balanced high-calorie diet to facilitate repletion of body fat and carbohydrates. Contact with the toxicant should be discouraged for at least four weeks after poisoning. Hemodialysis may be considered in poisoning by nitrophenolic compounds although extensive binding to plasma protein is characteristic. Another possibility in severe poisonings is exchange transfusion.

Chlorophenoxy Compounds (e.g., 2,4-D, 2,4,5-T)

Exposure may occur by ingestion, dermal exposure or inhalation.

Symptoms and Signs

These substances may irritate skin and mucous membranes causing coughing and burning sensations upon inhalation. Prolonged inhalation may cause dizziness. Ingestion of high concentrations may irritate the gastrointestinal tract. Vomiting, chest pain, abdominal pain and tenderness as well as diarrhea commonly follow, but neither ulceration nor perforation are typical. Systemic absorption of chlorophenoxy compounds may cause muscular twitching, skeletal muscle tenderness, muscle stiffness in the extremities as well as convulsions. The Guillain-Barre syndrome has also been reported; its appearance is suggestive of sensitivity since its occurrence is not always related to the exposure dose. Respiratory insufficiency from muscle weakness may have occurred in one accident victim. The prognosis after ingestion is usually good.

Laboratory Verification

Gas liquid chromatographic procedures may be used to measure chlorophenoxy compounds in blood and urine. Urine samples must be collected promptly because complete excretion may be accomplished in one or two days. These tests may be helpful in confirming and estimating the extent of chlorophenoxy absorption.

It has been reported that the oral ingestion of 5 mg per kg (350 mg per 70 kg) of 2,4-D by six healthy subjects led to an average peak plasma concentration of approximately 35 mg per liter at 12 hours with the average plasma half-life being 33 hours. No symptoms were reported. With respect to urinary concentrations, asymptomatic workers involved in 2,4-D application were found to have concentrations of 0.2 to 1.0 mg per liter. Treatment of suspected chlorophenoxy poisoning should not be delayed while waiting for confirmatory laboratory results so long as the medical history and clinical picture support the diagnosis.

Treatment

Decontaminate. Flush from contaminated skin, hair and eyes with large amounts of water. For ingestion, it may be necessary to induce emesis if this does not occur spontaneously and if the victim is fully alert. If consciousness is impaired, it may be necessary to lavage with 30 to 50 gm. of activated charcoal in 3 to 4 ounces of water, with appropriate precautions against hydrocarbon pneumonitis. Sodium sulfate may be used as a cathartic. Provide supportive care as needed (intravenous fluids, anticonvulsants, monitoring of hepatic, renal, and neurologic function). In severe cases, forced alkaline diuresis may be life saving.

Dithiocarbamates and Thiocarbamates

Exposure may occur via dermal contact, ingestion or inhalation.

Symptoms and Signs

Dermal contact may produce itching, redness and eczematoid dermatitis (the most common disability). Inhalation may occasionally produce nasal stuffiness, hoarseness, cough and (very rarely) pneumonitis. Sensitization may occur after repeated contacts. Ingestion may cause nausea, vomiting and diarrhea as well as low body temperature and ataxia. Muscle weakness and/or ascending paralysis may occur, with eventual respiratory paralysis. A combination of ethanol (beverage alcohol) and bis-dithiocarbamate may lead to flushing, sweating, headaches, a warm sensation, weakness, nasal congestion, difficult breathing, tightness in the chest, rapid heart rate and low blood pressure.

Diagnostic Features

If sensitization has occurred, skin testing may be useful. Detection of the intact pesticide in the blood is usually not feasible because of the rapid metabolism of the compounds. Ethylene thiouria may be readily detected in the urine after exposure to ethylene dithiocarbamates, however.

Treatment

Decontamination should be carried out by washing the skin and the hair with soap and water and gastric emptying by inducing of vomiting or lavage as appropriate. Sensitive persons should be removed from contact. The eyes should be flushed with clean water for 10 to 15 minutes. If thiram or dithiocarbamate compounds have been ingested, alcohol consumption is contraindicated for at least three weeks. Glucose containing fluid should be given intravenously to promote urinary excretion. Ascorbic acid, a hydrogen donor may have a significant antidotal action against dithiocarbamate compounds and may be included in the intravenous therapy. If an antabuse type reaction is occurring, oxygen can be administered. If respiration is depressed, however, oxygen may be administered by an intermittent positive pressure breathing device with close monitoring of pulmonary function. Gastric evacuation, charcoal administration, catharsis, and intravenous fluids may also be appropriate depending on the severity, the interval between exposure and treatment, and the amount of dithiocarbamate absorbed.

FUMIGANTS

Fumigants can present serious health hazards resulting in human illnesses and, occasionally, death. Methyl bromide, acrylonitirile, calcium cyanide and carbon tetrachloride are the fumigants most likely to cause death if over exposure occurs. Others which can cause skin and eye injury and systemic illness include:

-sulfuryl fluoride (Vikane®)
-1,3 dichloropropene (Telone®)
-1,2 dibromo-3-chloropropane (Nemagon®)
-ethylene dibromide
-formaldehyde
-chloropicrin
-phosphine
-sodium methyl dithiocarbamate (Vapam®)

Methyl Bromide

Methyl bromide is sold as a liquid under pressure. At atmospheric pressure it vaporizes at 40°F to a colorless and odorless gas. Because of this property, methyl bromide should always be used in formulations which contain chloropicrin (tear gas), which serves as a warning agent. A worker who is exposed to enough of this mixture to cause tearing has also been exposed to dangerous quantities of methyl bromide.

Methyl bromide is absorbed through the lungs, skin and mucous membranes. It can cause acute poisoning (either topical or systemic) and chronic effects.

Acute Poisoning

Topical Effects

Skin contact with the liquid or hign concentrations of the vapor produces itching and prickling of the skin. This is followed by redness and formation of vesicles and slow-healing blisters. Corneal ulceration may result from eye contact; dermal exposure to methyl bromide can be fatal.

In severe poisoning, the victim becomes comatose and has a high fever and respiratory embarrassment. Death is usually the result of either respiratory failure or cardiovascular collapse. Death is preceded by cyanosis, pulmonary edema, and renal failure. Muscle twitching and convulsions may occur. A potentially dangerous situation may develop if the possibility of a delay in the appearance of symptoms of acute poisoning is not recognized. The individual who has received a potentially fatal dose may not exhibit symptoms for 4-6 hours.

Chronic Effects

A papular pustular rash, not unlike acne, may develop on the face, arms, back and chest. This is the result of repeated dermal exposures. All the symptoms and signs under acute effects may also appear as a result of chronic exposure. Fatigability and loss of appetite are frequent complaints. More severe chronic manifestations include a change of personality, a chronic nervous system effect which may persist for years. Visual disturbances and locomotor impairment are common.

Case Presentation (Methyl Bromide)

The following case history of an agricultural worker exposed to methyl bromide is typical of behavioral manifestations which may be incurred with severe exposure to this fumigant.

The patient was a 50 y/o w/m who was working in the fields where methyl bromide had just been injected into the soil. His job was to ride on the back of a tractor and when torn sections of the plastic strip, which was being laid over the newly treated soil were noted, he would dismount and pull the edges of the plastic together and push them into the freshly treated soil, covering the hole in the plastic with more soil. In so doing, he sustained excessive exposure because of his hands getting into the soil and from inhalation of fumes emanating from the holes in the plastic. He wore no gloves or mask and was applying 98% methyl bromide and 2% chlorpicrin on a windy day.

Shortly after this exposure his employer noted that he appeared to be drunk because he was seen to be staggering, his speech was slurred and he was quite incoherent. He had taken no alcoholic beverages and in fact, had a three year history of complete sobriety. Four days later he was admitted to a local hospital because he was very disoriented, and was having hallucinations. He was disoriented as to time and place, and exhibited gross memory and intellectual impairment; he complained of a copper taste in his mouth. His moods varied between belligerency and calmness.

Physical examination of the CNS revealed that cranial nerves were within normal limits and the motor examination revealed normal strength and tone without drift. His sensory examination was intact to pinprick but his tendon reflexes were 2+ and the plantar response was flexor. A CAT scan of the brain was normal but the EEG was abnormal and demonstrated diffuse changes.

Laboratory studies showed normal renal studies but LDG, SGPT and SGOT were mildly elevated. Blood alcohol levels measured on his first day of admission were zero. He was admitted to the hospital to rule out metabolic encephalopathy, cerebral vascular insufficiency and possible vertebral basilar disease. The serum bromide level 12 days after exposure was 121 mg/L.

He was transferred to a mental institution because of the gross personality changes and his inability to look after himself.

Treatment

First, quickly get the patient out of the contaminated atmosphere and remove all contaminated clothing. Methyl bromide can penetrate ordinary rubber gloves (butyl rubber is preferred). Wash skin burns carefully with water. A therapeutic trial with dimercaprol (BAL) may be useful if given very soon after methyl bromide exposure. Keep the patient under observation for at least 48 hours after symptoms have subsided.

No simple laboratory tests are available for confirmation, but blood levels of bromine correlate well with the severity of the exposure.

Prevention

Methyl bromide must be applied by a closed-delivery system. Guards and warning signs should be posted. The application should be done at a safe distance from inhabited structures, and under appropriate weather conditions. Animals and humans must be removed from the area treated and should not be allowed back until a suitable clearance interval has passed.

Methyl bromide must be kept under lock except when the applicator or other responsible persons are present. The material should be stored in a cool, dry, well-ventilated building in order to avoid an explosion hazard and possible buildup of toxic concentrations of vapors caused by leaking containers. The storage sites should be at a safe distance from populated areas and inhabited buildings.

TOPICAL EFFECTS

Skin Problems Among Agricultural Workers

Skin problems accounted for 62% of all occupational diseases reported in the United States in 1973. The agricultural worker who is exposed to pesticides is four times more likely to develop a skin rash than the average industrial worker.

Diagnosis

Because the agricultural worker is exposed to a wide variety of agents besides pesticides, determining the cause of dermititis is highly complex.

Dermatitis from pesticides can result from: exposure to primary irritants, or contact with contact sensitizers (allergens)

The first diagnostic consideration is to differentiate between these two types of skin rash.

Primary Irritants

Absolute irritants are usually chemicals which can cause a chemical burn or severe irritation on almost anyone's skin. The reaction occurs immediately or within an hour or so. It usually does not present a diagnostic problem.

Relative irritants are agents which can cause varying degrees of dermatitis (inflammation of the skin) according to environmental conditions. Some, like kerosene or turpentine, are more likely to cause problems on sweating skin, or under occlusive clothing and boots. All are more damaging to skin which is already abnormal (sunburn, eczema and atopic dermatitis).

Some areas of the body are more susceptible than others. The genitalia, scrotum and eyelids are particularly vulnerable. Thus, a worker might have dermatitis on the penis and eyelids due to contamination by materials on the hands.

The primary irritants usually produce a short term dermatitis which goes away and can be related to a known definitive exposure.

The rash caused by primary irritants is more likely to be confined to the areas of the skin actually exposed to the chemical. Irritants in solution often are confined to the hands and the forearms, but relative irritants may be absorbed in clothing and boots. The rash will appear where the clothing is in closest contact with the skins--buttocks, knees and dorsum of the feet.

Irritants dispersed in sprays or aerosols more often affect the face and neck. Powders tend to accumulate at the waistline, the collar and tops of boots.

A primary irritant is likely to be the cause if several workers experience a rash on exposed surfaces at the same time, especially if burning and itching occurs soon after exposure. It is useful to ask the patient if he/she knows whether any other workers in the same area have the same problem.

When multiple cases of dermatitis follow the application of an agricultural chemical, the material or its carrier is clearly too irritating for continued use. The physician should be notified as soon as possible.

Treatment

When the person is removed from futher exposure, this type of dermatitis usually clears up, especially if a topical steroid cream is applied to the affected areas.

Contact Sensitizers

Substances which cause allergic contact dermatitis may affect only a few individuals who have become "sensitized" or "allergic" to the material. Even then, there may be marked differences between individuals in the degree of cutaneous reaction or severity of the clinical dermatitis.

A new product occasionally has a high potential for producing allergic skin conditions. These usually are soon recognized and taken off the market, but it is still worthwhile to ask whether a new product has been used. First reports of a hazardous substance often come from nurses or other medical personnel who are closest to field conditions.

Depending on the patient's sensitization, the reaction may occur within a few hours of contact or as long as a week later. Most occur within 48 hours. Redness, itching, swelling (especially around the eyes), and "water blisters" are the clues to this type of dermatitis.

Having a basic knowledge of the prinicipal sensitizers, reading the ingredients on the labels, or checking the Physicians' Desk Reference will often help in diagnosis. Plant dermatitis is common and must be considered as a cause of allergic contact dermatitis.

Some chemicals may be both primary irritants and contact sensitizers. In addition, many agricultural compounds are dissolved in solvents such as kerosene or xylene. This creates a perfect mechanism for both primary skin damage and an allergic reaction.

Treatment

The treatment of allergic contact dermatitis includes:

-using cold compresses
-treating infections
-identifying the offending agent

It may be necessary to refer the patient to a facility which performs patch testing.

Topical steroid creams, gels or lotions are beneficial. Severe or extensive cases may require a short course of systemic steroids. Systemic steroid therapy should always be under the direction of a physician. It should never be given to patients who may have undetected tuberculosis or are at risk of tuberculosis.

Apart from the highly specialized area of patch testing, the laboratory has no place in the verification of topical skin effects from pesticides.

The illnesses are often a sensitivity phenomenon and are therefore not strictly dose-related. Cholinesterase determinations and urinary metabolite studies are not necessary.

Effects of Pesticides on the Eyes

Eye injuries are common in agricultural workers. Topical effects can occur as the result of exposure to any of the pesticides in common use today. In addition, xylene and petroleum distillates in common use as pesticide carriers are very irritating materials. They produce a severe inflammatory response when they get into the eyes.

Eye injuries can result from:

accidentally splashing or spilling the
material into the eye,
exposure to pesticide drift, and
rubbing the eyes with contaminated hands.

Sulphur, paraquat, omite, parathion and dieldrin are some of the most common causes of eye injuries.

Eye injuries are most common in pesticide mixers, loaders and applicators because of their risk of exposure to the pesticide concentrate.

Damage is the result of:

a direct irritating effect of the chemical or the vehicle,
an allergic reaction, or
direct pharmacologic action on the eye (anticholinesterase pesticides.)

Conjunctivitis, corneal ulceration, uveitis and lenticular opacities are some of the lesions which occur. These chemicals have a delayed effect on visual accomodation and diminish the peripheral fields of vision.

First Aid

If there is a conjunctival infection, irrigate the eyes from the inside to the outside with large amounts of water or sterile normal saline solution. After the eyes have been thoroughly irrigated, evert first the upper and then the lower lid and clean them with a moist cotton tip to remove any debris. Then irrigate the eyes once more. Apply an eye shield and make an appointment for the patient to see the attending physician for definitive diagnosis and treatment.

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TABLE 1. CLINICAL ASPECTS: SUMMARY OF SIGNS, SYMPTOMS AND TREATMENT

	Organophosphates and Carbamates
Symptoms and Signs	MILD. Headache, fatigue, dizziness, blurred vision, sweating, abdominal cramps, vomiting, diarrhea, salivation, miosis. MODERATE. Chest discomfort and tightness, slow heart rate, muscular twitching, confusion, ataxia, slurred speech, bizarre behavior. SEVERE. Local or generalized seizures, loss of deep tendon reflexes, shock, cardiac rhythm disorders, impaired pulmonary function. On set of acute poisoning is usually within 15 minutes to 1 hour of contact but may be delayed for 4 to 12 hours.
Treatment	1. Establish airway. Support respiration and circulation. Death is usually due to respiratory failure. 2. If poisoning is severe, inject atropine sulfate IV (or IM if IV is impossible) after overcoming cyanosis. Use 0.4 - 2.0 mg for adults and 0.05 mg/kg for children. Repeat every 15 - 30 minutes until patient is atropinized (dry mouth, flushing, midriasis, tachycardia). 3. In severe organophosphate poisoning for adults, inject 1.0 gm of Pralidoxime chloride (2-PAM, Protopam® chloride) IV (or IM if IV is impossible) at no faster than 0.5 gm per minute. Repeat in 1 hour if nicotinic toxicity persists. In children under 12 years, give 20 - 40 mg per kg, injecting no more than half the total dose per minute. Repeat every 10 to 12 hours as indicated, up to two or three times. 4. Decontaminate as appropriate. For skin contact, carefully remove patient's clothing (wear rubber gloves). Carefully wash skin and hair with soap and water and clean under nails. Avoid contact. For ingestion, decontaminate with the induction of vomiting, lavage, and installation of activated charcoal as indicated.

TABLE 1. (continued)

	Chlorinated Hydrocarbons	Bipyridils
Signs and Signs	Nausea and vomiting, apprehensions, excitability, twitching, tremors, mental disorientation, weakness, parathesive, convulsions, respiratory depression. Onset of acute poisoning usually within 20 minutes to four hours of exposure.	EARLY burning of mouth, oral ulcerations, substernal and abdominal pain, vomiting, diarrhea, myalgia. DELAYED (48-72 hours) oliguria, jaundice, cough, respiratory distress, convulsions, coma. Severe delayed illness may be preceded by mild early symptoms.
Treatment	1. Decontaminate. For ingestion, induce vomting or lavage stomach with 2-4 liters of tap water as indicated. Instill 30 gm of activated charcoal in 3 - 4 oz of water. Sodium sulfate may be used as a cathartic. 2. Maintain respiration and circulation. Treat seizures and other problems as indicated. 3. Avoid oils, oil laxatives, and stimulation by chemical, physical or other means.	1.Decontaminate.Flush from contaminated skin, hair and eyes with large amounts of water. For ingestion, lavage with at least 2 liters of normal saline or 5% sodium bicarbonate. Instill a slurry of 8 to 10 oz of Fuller's Earth. May use catharses when patient can tolerate food ingestion. Avoid contact with contaminated materials. 2. Do not administer supplemental oxygen. 3. Forced diuresis, hemodialysis and hemoperfusion with activated charcoal.

	Chlorophenoxy Compounds	Thiocarbamates
Symptoms and Signs	Coughing and burning sensations, dizziness, vomiting, chest pain, abdominal pain and tenderness, diarrhea, muscular twitching, skeletal tenderness, muscle stiffness of extremities, convulsions, Guillan-Barre syndrome.	WITHOUT ALCOHOL INGESTION. Itching, redness, dermatitis, hoarseness, coughing, nausea, vomiting, ataxia, muscle weakness, paralysis. WITH ALCOHOL INGESTION. Flushing, sweating, shortness of breath, chest pain, hypotension

TABLE 1. (continued)

	Chlorophenoxy Compounds (continued)	Thiocarbamates (continued)
Treatment	1. Decontaminate. Flush from contaminated skin, hair and eyes with large amounts of water. For ingestion, induce vomiting or lavage with tap water as indicated. Instill 30 gm activated charcoal in 3 - 4 oz of water. Sodium sulfate may be used as a cathartic (15 gm in 6-8 oz of water).	1. Decontaminate. Wash skin and hair; flush from eyes; empty stomach by induction of vomiting or lavage as appropriate; instill 30 gm of activated charcoal in 3 - 4 oz water and use sodium sulfate cathartic as required. 2. IV fluids to promote urinary excretion.
	2. Provide supportive care as needed (intravenous fluids, anticonvulsants, monitoring of hepatic, renal, and neurologic function).	3. If complicated by alcohol, oxygen as needed and Vitamin C (1 gm at rate not exceeding 0.2 gm/ minute for adults and children over 12 years).
		4. No alcohol for 3 weeks in any case.

	Methyl Bromide Fumigant
Symptoms and Signs	SYSTEMIC. Delayed onset common. Dizziness, nausea, vomiting, headache, blurred vision, changing taste of food, listlessness, weakness, staggering gait, slurred speech, temporary blindness, fever, respiratory embarrassment, coma, cardiovascular collapse, renal failure.
Treatment	1. BAL may be useful especially if given before symptoms appear. 2. Remove from exposure and decontaminate. Wash skin and hair; flush from eyes/ be aware that ordinary rubber gloves may not be impervious. 3. Keep physical activity of patient to a minium. 4. Provide appropriate support for cardiovascular, respiratory, central nervous system, etc.

SUGGESTED FORM FOR COLLECTION OF ACUTE POISONING LABORATORY SAMPLES

Submit ALL of the following samples to the toxicology labs as soon as possible, or at least WITHIN 24 HOURS.

Label EACH with name of patient, physician and hospital, collection time and date.

CONTAINER: Obtain the container in which the poison is stored.

BLOOD #1: Draw 5 cc in BD green-topped (heparinized) vacutainer tube. NEVER freeze this sample. This sample CANNOT be shipped with Dry Ice.

BLOOD #2: Draw 10 cc in a BD red-topped vacutainer tube. If whole blood cannot be submitted to the lab within 36 hours, separate the serum and ship the SERUM frozen. DO NOT freeze whole blood.

URINE #1: Obtain 20 cc of the first grab sample available after the poisoning episode has occurred. Collect in a GLASS container. Line the lid of the container with CLEAN ALUMINUM FOIL. SEND IMMEDIATELY or freeze and send as soon as possible.

OTHER URINES: Obtain 20 cc of FIRST MORNING VOID each day until instructed otherwise. SEND IMMEDIATELY or freeze and send as soon as possible.

VOMITUS OR GASTRIC LAVAGE: Collect 10 cc of vomitus or FIRST GASTRIC LAVAGE (ONLY IF vomitus is unavailable). SEND IMMEDIATELY or freeze and send as soon as possible. If this sample is left standing at room temperature over 3 hours, it is of NO VALUE.

FOR MEDICAL CONSULTATION CALL:

FOR LABORATORY INFORMATION CALL:

SEND LABORATORY SAMPLES TO:

MAILING INSTRUCTIONS:

Chapter 9

Laboratory Verification

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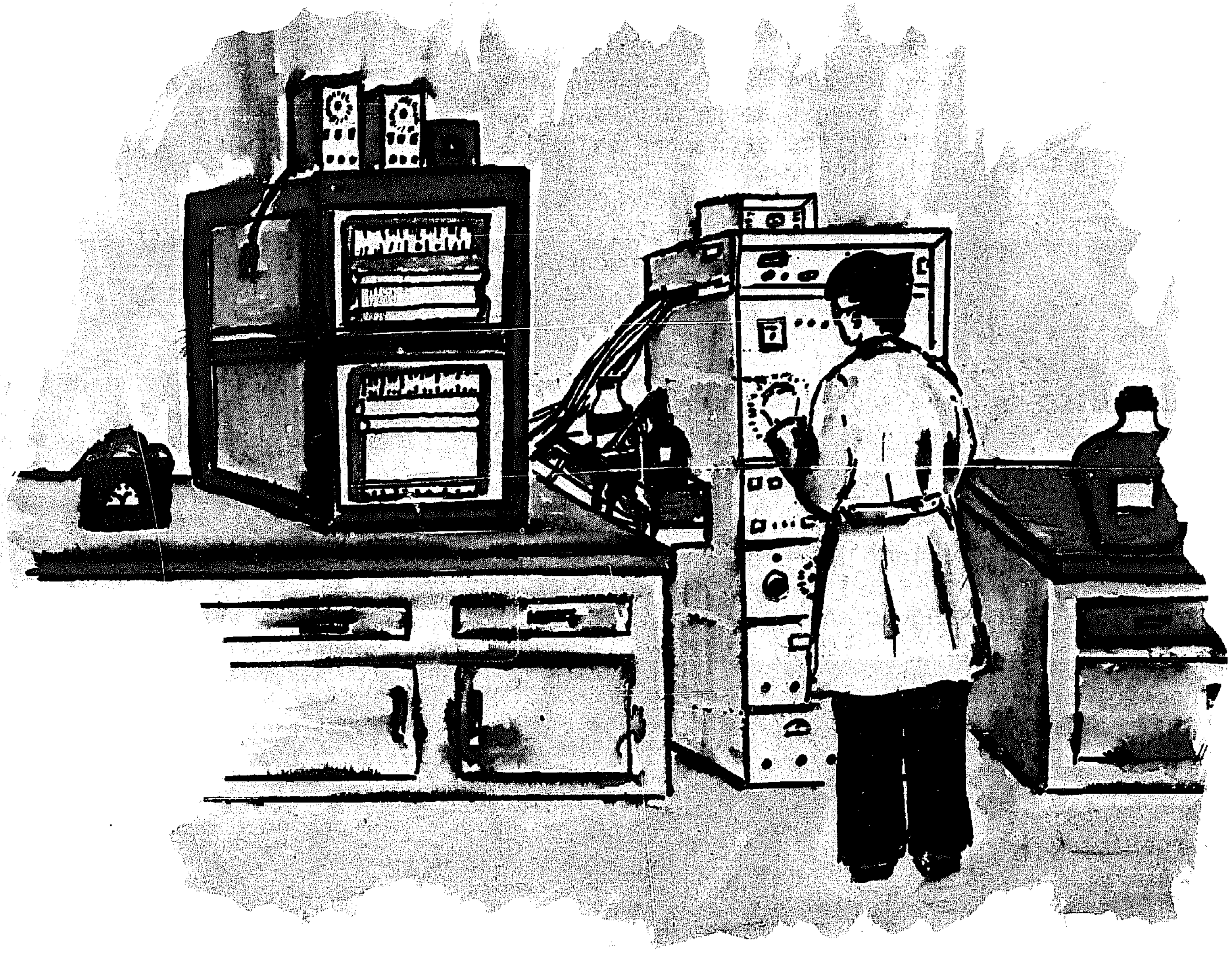


SUMMARY

Laboratory analysis is needed for verification of suspected pesticide poisoning. Analytical methods for an extensive number of pesticides and their metabolites have been developed.

INTRODUCTION

When the medical history and samples reach the toxicology laboratory they are used in the following ways:

1. The patient's health and exposure history is used to assist the toxicological chemist in planning several analyses.

2. The contents of the pesticide container are examined for intact pesticide residues.

3. The vomitus or gastric lavage is analyzed for intact pesticide content.

4. The blood is examined for:
    a. Cholinesterase activity
    b. Intact pesticide content

5. The urine is examined for metabolic products derived from intact pesticides; these may be:
    a. Specific for a particular pesticide
    b. Indicative, as of a class of pesticides, such as the organophosphates (OPs).

Analyzing the Contents of the Pesticide Container:

The bulk of intact pesticides can be analyzed by gas chromatography (Sherma, 1975; Thompson, et al., 1977) or combined as chromatography/mass spectrometry, even at extremely low concentrations. Table 9-1 is a partial list of some pesticides which can be readily quantified by using gas chromatography. Even if the container appears empty, it will usually contain enough material to lead to a positive identification of the toxic agent. This approach is rapid and helps the toxicologist plan the rest of the analyses on other samples submitted to the laboratory.

Table 9-1. Some Pesticides and Their Metabolites Which Can Be Quantified by Gas Chromatography

Mevinphos
Tecnazene
2,4-D (ME)
Hexachlorobenzene
α BHC
CDED
2,4-D (IPE)
lindane
chlordane
β BHC
Diazinon
PCNB

2,4,5-T (ME)
heptachlor
2,4,5-T (IPE)
dimethoate
Ronnel
Aldrin
1-hydroxychlordane
Oxychlordane
methyl parathion
heptachlor epoxide
DCPA

Malathion
o,p'-DDE
γ Chlordane
α Chlrodane
trans-Nanochlor
ethyl parathion
Endosulfan I
p,p'-DDE
DDA (ME)
o,p'-DDD
dieldrin
o,p'-DDT

endrin
p,p'-DDD
chlordecone
Endosulfan II
Ethion
p,p'-DDT
Carbophenothion
Methoxychlor
Mirex
endrin
Tetradifon

Analyzing Vomitus or Gastric Lavage:

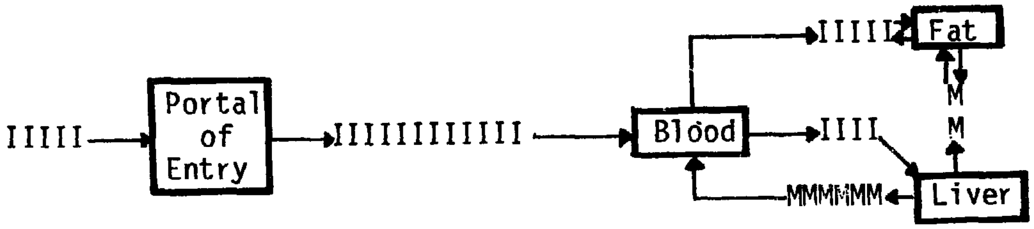
Vomitus or gastric lavage is useful to identify intact pesticides. Usually a simple extraction of the material with an organic solvent (benzene) will afford an analytical sample which can be analyzed by gas chromatography after it has been passed through a small column of silica gel. If either type of sample is allowed to stand in the hospital or clinic at room temperature for more than three hours, the sample will probably be too deteriorated to yield a positive identification of the toxic agent.

Many pesticides decompose in the presence of water, acid, base and/or light. Care must be used to freeze a vomitus or lavage sample as soon after collection as possible.

Positive identification of an intact pesticide in blood serum is a bit more difficult than in the samples discussed above. Moreover, in blood, organochlorine pesticides (OC's) behave differently than do organophosphorus and carbamate pesticides. Consequently OC's will be discussed separately.

Analyzing Blood for Organochlorine Pesticides:

An organochlorine pesticide is readily absorbed through the skin, lungs and alimentary tract. It enters the bloodstream, and a concentration equilibrium is established between the fatty constitutents of blood and other fatty tissues, especially depot fat. The organochlorine pesticides are not very water soluble and do not react readily with water. When acute exposure to an OC pesticide occurs, the bloodstream becomes overloaded with intact pesticides (I). The liver metabolizes some of the OC(M) and the fat sequesters some of the intact material and some of the metabolite(s):



Eventually most of the OC pesticide and metabolite(s) become sequestered by the adipose tissue. After all sources of exposure are removed, the serum metabolites are slowly removed by the kidneys. Polychlorinated biphenyls (PCB's), although not pesticides, are also sequestered by fat and may confound some OC analyses. Table 9-2 contains many of the organochlorine pestices and organochlorine metabolites detectable in blood (Dale, 1966).

Table 9-2. Some Organochlorine Insecticides and Their Metabolites Which Are Detectable in Human Blood*

p,p'-DDT	o,p'-DDD	Aldrin	Heptachlor Epoxide
o,p'-DDT	α BHC	Dieldrin	Oxychlordane
p,p'-DDE	β BHC	Endrin	Mirex
o,p'-DDE	γ BHC	Heptachlor	Hexachlorobenzene
p,p'-DDD	δ BHC		

*PCBs are also detectable

The most documented exposures to organochlorine pesticides are those involving DDT. Absorbed DDT is converted into DDE in the liver and stored as DDE and intact DDT in adipose tissue. Serum DDE is slowly converted to water soluble metabolites and eliminated in the urine. DDT is also converted to DDA which is also eliminated by the kidneys. Metabolite excretion disturbs the fat/blood equilibrium concentrations of pesticide and DDE. This causes more DDT and DDE to enter the bloodstream and eventually the liver. The process continues until the DDT and DDE stores become depleted.

Other OC pesticides behave similarly but establish different fat/blood equilibria. Most OC's are eliminated more rapidly than DDT and DDE.

In instances of acute poisoning, the level of the OC pesticide involved is in significant excess to the level observed for the population in general. Thus, DDT ingestion can lead to a blood concentration several orders of magnitude higher than those reported for the general population today.

The more volatile halogenated organic compounds have also been detected in exposed humans. Chloroform, carbon tetrachloride, trichloroethylene, tetrachloroethylene, *cis*-1,2-dichlorethylene, 2,3-dibromochloropropane, methylene bromide and methyl chloroform have all been detected in individuals either occupationally or accidentally exposed to the materials.

Analyzing Blood for Organophosphorus and Carbamate Pesticides:

Organophosphorus and carbamate pesticides are specifically designed to degrade rather rapidly in aqueous media so as not to constitute a persistent threat to the environment. It is thus often possible to detect intact OP's or carbamates in vomitus but fail to find them in serum. Likewise, cholinesterase depression (discussed later) is quite often detected although the analysis of blood for intact pesticide is negative. For those types of compounds, the more lengthy urinary analyses have become of primary importance. However, if a sample of blood has been collected within a few hours after acute exposure, the intact pesticide can often be identified easily and rapidly. This is important to emergency room personnel, and the procedure should be practiced when possible. Often it is difficult to obtain urine samples just after an episode; this leads to long delays in the requested verification of the toxic incident.

Anaylzing Urine for Organophosphorus, Carbamate and Other Pesticides:

Urinary analyses are important alternate ways of verifying exposure to most types of pesticides except OC's. These procedures require extensive laboratory time and cannot be considered rapid methods. Table 9-3 contains a number of pesticides along with the urinary metabolites for which analytical methods have been established (Shafik, 1971; 1972; 1973). Table 9-4 defines the abbreviations appearing in Table 9-3.

In the case of organophosphorus pesticides, one fragment (actually sometimes several related fragments) may be utilized to confirm that a poisoning agent belongs to a this class of compounds. However, all fragments must be identified if the absolute identity of the pesticide is important as in court cases.

An OP pesticide may be pictured as composed of a dialkyl moiety and a large leaving group:

dialkyl phosphate —— bulky leaving group

The dialkyl portion is usually methyl or ethyl, thus most OP's yield either dimethyl or diethyl phosphates. Actually the situation is a bit more complex, in that either of the two oxygens of the phosphate portion may be substituted by sulfur, so that in addition to dialkyl phosphates, dialkylthiosphosphates and even dialkylphosphorothioates may be formed from the sulfur containing analogs. Table 9-5 indicates which major dialkyl phosphate metabolites arise from which organophosphorus pesticides.

Table 9-3. Some Pesticides and Their Corresponding Urinary Metabolites for Which Analytical Methods Have Been Established

Pesticide	Urinary Metabolite(s)
Captan (Merpan®)	THPI
Carbaryl (Sevin®)	1-Naphthol
Chlorfenvinphos (Birlane®)	DEP, DETP, desethylchlorfenvinphos
Chlorpyrifos (Dursban®)	DEP, DETP, 3,5,6-trichloro-2-pyridinol
Demeton (Systox®)	DEP, DETP, DEDTP
Diazinon (Spectracide®)	DEP, DETP
Dichlorfenthion (VC-13®)	DEP, DETP, 2-4-dichlorophenol
Dichlorvos (DDVP)	DMP
Dicrotophos (Bidrin®)	DMP
Dimethoate (Cygon®)	DMP, DMTP, DMDTP
Ethion (Nialate)	DEP, DETP, DEDTP
Ethyl bromophos (Nexagen®)	DEP, DETP, 2,5-dichloro-4-bromophenol
Ethyl parathion (Niran®)	DEP, DETP, PNP
Fenchlorphos (Ronnel)	DMP, DMTP, 2,4,5-trichlorophenol
Fenthion (Baytex®)	DMP, DMTP
Malathion (Cythion®)	MCA, DCA, DMP, DMTP, DMDTP
Mancozeb (Dithane®)	ETU
Methyl bromophos (Nexion®)	DMP, DMTP, 2,5-dichloro-4-bromophenol
Methyl parathion (Metaphos)	DMP, DMTP, PNP
Monocrotophos (Azodrin®)	DMP
Naled (Dibrom®)	DMP
Phorate (Thimet®)	DMP, DMTP, DMDTP
Propoxur (Baygon®)	IPP
Trichlorphon (Dipterex®)	DMP

Table 9-4. Definitions of Urinary Metabolite(s) Abbreviations

Abbreviations			
THPI	tetrahydrophthalimide	DMDTP	dimethyldithiophosphate
DEP	diethylphosphate	PNP	paranitrophenol
DETP	diethylthiophosphate	MCA	monocarboxylic acid
DEDTP	diethyldithiophosphate	DCA	dicarboxylic acid
DMP	dimethylphosphate	ETU	ethylenethiourea
DMTP	dimethylthiophosphate	IPP	2-isopropoxyphenol

Table 9-5. Some Pesticides and Their Major Metabolites

Pesticides	Oral LD_{50} mg/kg	$Dermal_{50}$ mg/kg	Metabolites
I. <u>Dimethyl Organophosphates - Alkylphosphates</u>			
Mevinphos	7	5 - 33	DMP
Methyl parathion	9 - 25	67	DMP, DMTP
Dichlorvos (DDVP)	56 - 80	75 - 107	DMP
Dimethoate (Cygon®)	215		DMP, DMTP, DMDTP
Naled (Dibrom®)	430	1,100	DMP
Malathion	1,000-1,375	4,000	DMP, DMTP (minor metabolites)
II. <u>Diethyl Organophosphates</u>			
Ethyl parathion	3 - 33	21	DEP, DETP
Chlorpyrifos (Dursban®)	135	2,000	DEP, DETP
Dichlofenthion (VC-13®)	270	6,000	DEP, DETP
Diazinon	100 - 150	900	DEP, DETP

Urinary dialkylphosphate analyses narrows down the list of possible organophoshate toxic agents but does not completely identify the specific compound. Thus, if only DMP is found in urine, suspect OP pesticides would inlcude: dichlorvos (DDVP), dicrotophos (Bidrin®), mevinphos (Phosdrin®), monocrotophos (Azodrin®), naled (Dibrom®) and trichlorphone (Dipterex®). If both DMP and DMTP are discovered, the possible candidates include: fenchlorphos (Ronnel), fenthion (Baytex®) and methyl bromophos (Nexion®). However the latter compound would yield 2,5-dichloro-4-bromophenol which is detectable by another procedure.

Similarly, methyl parathion yields paranitrophenol in addition to DMP and DMTP. Dimethoate (Cygon®) and phorate (Thimet®) and malathion (Cythion®) all yield DMP, DMTP and DMDTP. The latter compound is usually confirmed by special urinary analysis for the corresponding mono- and di-carboxylic acids of malathion.

Some DEP/DETP combinations include chlorfenvinphos (Birlane®), chlorpyrifos (Dursban®), demeton (Systox®), diazinon (Spectracide®), dichlofenthion (VC-13®), ethion (Nialate), ethyl bromophos (Nexagen®) and ethyl parathion (Niran®). Distinction between many of these candidates can be made by separate analyses for urinary phenols such as 3,5,6-trichloro-2-pyridinol, 2,5-dichloro-4-bromophenol and paranitrophenol.

Two carbamate pesticides which yield useful urinary metabolites include carbaryl (Sevin®) which gives 1-naphthol and propoxur (Baygon®) which yields 2-isopropoxyphenol.

A few pesticides have special metabolites of current interest. Captan (Merpan®) residues can be detected by urinary analysis for tetrahydrophthalimide and mancozeb (Dithane®) residues can be traced by urinary analysis for ethylenethiourea.

CHOLINESTERASE

Analyzing Blood for Cholinesterase Activity:

Biochemical Basis of Cholinergic Illness

The poisonous effects of organophosphorus and carbamate pesticides come about through inhibition of cholinesterase, a rather large enzyme (molecular weight around 260,000 Daltons) produced in the liver. Cholinesterases are categorized by their ability to break down certain substrates. One form, acetylcholinesterase, is present at the neurosynaptic junctions where it breaks acetylcholine into acetyl and choline fragments. Its function is to increase the precision of nerve firing, enabling some nerve cells to fire as rapidly as 1,000 times per second without overlap of the neural impulses. A second form of the enzyme, commonly known as pseudocholinesterase and clinically known as butyryl cholinesterase is primarily located in the plasma and pancreas, although small quantities of it exist in all human tissues. The term pseudocholinesterase was used in the past because for many years the form appeared physiologically inert in humans. Today, butyryl cholinesterase is thought to assist acetylcholinesterase in controlling neurosynaptic firing as the impulse frequency approaches maximum values. In such circumstances the levels of acetylcholine produced inhibit the action of acetylcholinesterase but not that of butyryl cholinesterase. Inhibition of the enzyme, which is assessed as a percentage change in enzymatic activity, is categorized according to one of two processes by which the inhibition can occur.

Carbamate insecticides inhibit cholinesterase (ChE) activity in reversible fashion. Because they interact with ChE by weak, ionic chemical bonding, the enzyme ususally regenerates itself spontaneously. The half-life of this spontaneous regeneration, the time required for half of the enzymes to reactivate, is on the order of minutes to hours and is dependent on the nature of the specific carbamate involved, the dosage received and the length of exposure. Use of 2-PAM (pralidoxime chloride) to counteract ChE depression is contraindicated in cases of acute carbamate exposure because the 2-PAM inhibits the sponstaneous enzymatic regeneration just described.

Organophosphorus pesticides inhibit cholinesterase by forming covalent chemical bonds through a process called phosphorylation. Spontaneous enzymatic regeneration half-lifes are, in these cases, days to months long. As with carbamates, the nature of the OP involved, the dose received and the duration of exposure all affect the period for regeneration to occur. Because of the prolonged regeneration half-lifes, organophosphorus intoxication is usually considered more serious although some exposures to carbamates lead more rapidly to symptomatology and can indeed be just as lethal. Organophosphates affect both RBC and plasma ChE activity whereas carbamates normally affect only the plasma fraction.

Biochemical Assessment of Cholinergic Depression:

Biochemical assays designed to study purified forms of the enzymes have not only enlightened researchers as to the functional capacity of cholinesterases, but have also enabled chemists to establish guidelines for performing blood and urine analyses on afflicted individuals. The amount of an enzyme in a given solution or tissue extract can be assayed quantitatively in terms of the metabolic capacity of the enzyme. From such information a fairly quantitative, direct assessment of the chemical condition of an individual may be made. As examples, a change of 0.1 ΔpH unit/hour (Michel method) would not be considered critical whereas a change of 0.3 unit would be. Normally an activity depression of more than 30% is considered life-threatening, although individuals vary widely in their pesticide exposure tolerances.

Clinical assessment cannot, however, await laboratory results. Cases involving acute exposure to pesticides must be treated immediately and agressively if the patient is to survive. Laboratory results are confirmatory tools and a means of verifying patient response to treatment.

If facilities for blood fraction analysis are unavailable and the patient's blood must be sent out for cholinesterase activity evaluation, care must be taken to ship the material correctly as outlined early in this Chapter. Also, a process known as "aging" must be kept in mind when the time comes to interpret laboratory results. Aging is a function not only of time but of chemical structure and is related to the stereochemistry of the phosphorylated enzyme. Chemical rearrangement can occur around the active site of the enzyme and preclude any chance of spontaneous regeneration. Aging may cause the numerical values which represent enzyme viability to be extremely low. This, in turn, will make it difficult to interpret the results and assess the true status of the patient. Moreover, after aging has occurred, response to 2-PAM or atropine medication will be minimal. Inasmuch as "aging" is temperature and pH dependent, samples should be maintained at 4°C during transportation and shipment. The time course for aging is 2-4 days.

Laboratory Analysis of Cholinergic Depression:

Several laboratory methods (Ellman, 1961; Michel, 1979)and even one field test method exist for assessment of cholinesterase activities. Table 9-6 lists these methods, the lower limits of normal plasma and RBC cholinesterase activities of human blood and the units employed to report values arrived at from following these procedures.

Table 9-6. Approximate Lower Limits of Normal Plasma and Red Blood Cell Cholinesterase Activities in Humans [a]

Method	Plasma	RBC	Units
ΔpH/hour (Michel)	0.4	0.5	ΔpH/hour
pH STAT (Nabb Whitfield)	2.3	8.0	μm per ml per minute
ChE-tel (Pfizer)	40		ChE-tel units
A ChE-tel (Pfizer)	---	210	A ChE-tel units
1-Test Cholinesterase (E.M. Diagnostics)	3.6	---	Units per ml
Acholest Test Paper	20	---	Minutes
Dupont ACA	8	---	Units per ml
Garry-Routh (Micro) Male	7.8	---	
Female	5.8	---	M-SH per ml per 3 min.
Merckotest	3.0	---	Units per ml

[a] Because measurement techniques vary among laboratories, more accurate estimates of minimum normal values are usually provided by the individual.

The Acholest field procedure is for qualitative analysis of cholinergic depression. It employs a stripbound substrate which produces protons (H+) proportionate to the enzymatic activity of the sample being tested. The protons influence color change by a pH-sensitive indicator. Interpretation is by visual comparison with a printed color chart.

One of the most useful and widely applied ChE procedures is the Michel method. By the use of a pH meter, changes in pH of a known amount of either RBC or plasma acetylcholine are measured over time. As acetylcholine is cleaved, acetic acid is generated. This acid changes the pH of the test solution and the magnitude of the change in pH is measured as a function of time, hence the units of ΔpH/hr.

Every hospital emergency room and migrant clinic that receives acute pesticide poisoning cases should be prepared to assess cholinesterase activity through an acceptable procedure such as the Michel method.

Helpful Suggestions Regarding the Michel Method

Several important recommendations will now be made regarding the use of buffer solutions and pH meters.

Buffers:

A. Stock solutions, those diluted just prior to use, must be made up under sterile conditions.

B. Bottles used for storage of buffer solutions should first be washed with detergent and multiply rinsed (6 to 8 times) with pure de-ionized water, when available.

C. Solutions should be stored at 4°C to minimize bacteria growth. (Multiple sample withdrawal introduces bacteria into all buffers.)

D. Any preservative added to a buffer must be comparable with the assay of interest, especially causing no interfering responses.

pH meters:

A. Always make certain that the level of reference solution (aqueous KCl) is slightly below the opening in the electrode which permits constant equilibrium with atmospheric pressure.

B. Unless specified to the contrary, keep a little solid KCl visible in the reference solution of the electrode to insure that it is saturated.

C. Prior to calibrating the meter, all solutions must be within the recommended temperature limits.

D. The meter must read, at the sensitivity settings chosen and the operating temperature, all three pH ranges accurately without requiring further adjustment.

E. The pH values of 4.0, 7.0 and 10.0 should be obtainable accurately with less than 60 seconds delay between each reading.

F. Electrodes must be thoroughly rinsed with distilled water and dried before and after each use.

G. Electrodes should soak overnight in a solution of 0.1M HCl.

H. If electrodes are not used for several days, they should be immersed in a 0.5M buffered solution of neutral pH.

Table 9-7 contains a complete list of the apparatus and reagents needed to determine RBC and plasma cholinesterase activities by the Michel method. Normal ranges for these activities according to this procedure are:

Red Blood Cells: 0.57 - 0.98 ΔpH/hour
Blood Plasma: 0.53 - 1.24 ΔpH/hour

As previously mentioned, whereas organophsophorus pesticides affect both the RBC and the blood plasma, carbamates generally affect only the plasma. Depressed ChE activity as low as 0.07 ΔpH/hr has been observed for plasma. Greater than 30% depression of ChE activity in either blood fraction must be given serious consideration.

Table 9-7. Apparatus and Reagents Needed for Determination of Red Blood Cell and Plasma Cholinesterase Activity

Apparatus	Approximate Cost
Analytical balance	$1,500
pH meter (+ electrode)	500
Centrifuge	200
Beakers (5 ml)	10/pkg of 12
Oxford pipettor (20 microliter)	50
Oxford tips (disposable)	36/per 1,000
Pipets (serological 0.2 ml)	3 each
Pipets (transfer 1 ml)	35/per 18
Stopwatch or clock with second hand	30
Pasteur pipets (disposable)	3.50/gross(144)
Rubber bulbs for disposable pipets	3
1000 ml volumetric flask for buffer	15 each
100 ml volumetric flask for substrate	7 each
Blood Collecting Materials	
Heparinized vacutainer tubes (10 ml)	14.50/100
Syringes (20 cc)	10.80/pk of 25
Tourniquet ($4.50, alcohol swabs, band aids, labels)	
Reagents	
Using the amounts listed below, one could perform in excess of 500 tests	
Buffer	
Sodium barbital	25 g = $3.40
Potassium dihydrogen phosphate	100 g = 2.10
Potassium chloride	250 g = 2.90
Sodium chloride	500 g = 2.10
Hydrochloric acid	500 ml = 7.00
Substrate (stays fresh for approximately one month)	
Acetylcholine chloride	5 g = 2.40
Other	
Saponin	25 g = 2.40

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Chapter 10

Human Pesticide Exposure Assessment

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SUMMARY

The medical concerns of human pesticide exposure are changing. Whereas until recently, as in the United States, acute pesticide poisoning was the main focus. Today attention is also turning to chronic exposures and ways in which these can be reduced. This Chapter describes techniques, both direct and indirect, to measure exposures and compares the specificity of exposure estimates which are based upon biologic indices of exposure with those that are really proxy indicators of exposure.

INTRODUCTION

Initially, the major medical concerns of pesticide management were pesticide poisonings and how they could be prevented. Over the last decade, however, as has been described in Chapter 3 on Pesticide Epidemiology, we have noted a variety of different diseases which have been associated with chronic as well as acute exposures and ways in which both can be reduced.

This chapter describes techniques both direct and indirect to measure exposure and ways in which personnel can be monitored. The specificity of exposure estimates which are based. on biologic indices are contrasted with the less precise estimates of exposure such as person years, occupational categories, etc. which have to be used in long-term studies of the pesticide worker.

In this Chapter, however, we are more concerned with human pesticide exposure, how this is measured in the laboratory in short induction diseases such as acute poisonings, and how exposure is measured in more chronic situations; here the problems of multiplicity of chemical exposures and their interactions with each other and with lifestyle characteristics, become important considerations for the risk of chronic diseases with long induction times.

Pesticide Exposure Assessment of the Worker

Historically, human exposure to a wide variety of pesticides has been quantitated in several occupational groups by two research methods. These are:

Direct Methods — Indirect Methods (biologic indices)

Direct Methods

Direct methods were the first methods used to measure worker exposures to pesticides and alpha cellulose patches were used for spray exposures and layered gauze patches for dust exposures. In addition, T-shirts were used and for hand exposures the cloth bag rinse technique (Durham and Wolfe, 1972). More recently, because of interfering peaks being found with T-shirts and because of the high cost of solvents, multiple patches have been used to measure dermal exposures and respiratory exposures have been quantitated by measuring the amount of special filter pads held in single unit respirators (Davis, 1980). These direct methods have been used to measure the exposures of mosquito control workers to fenthion, structural pest control operators to carbaryl, field spraymen to parathion, and many other worker exposure situations.

When conducting these field exposure studies, because they are costly, it is important to be sure that there are no problems of interference in the materials to be used to trap and measure the pesticide exposures. Alpha cellulose patches have been found to be relatively free from interference problems, and these patches should be glassine backed and placed on the worker's clothing for a definite period of time. Then a 25 cm^2 area of the patch should be cut out and placed in a methylene chloride solvent in the field. The latter step facilitates recovery of most of the pesticide residue and the specimen should then be packed in dry ice and shipped to the laboratory for subsequent chemical analysis. Pesticide or metabolite concentrations should be expressed in mg/cm^2/hr.

The number and anatomical locations of patches will vary with the work characteristics under study. Thus, the hands and arms will be the most exposed area of the body when working with low growing row crops. Whereas, in cotton, the legs and arms sustain the greatest exposure so the alpha cellulose patches should be taped onto these parts of the body. In the citrus grove, the whole body is at risk of exposure and, here, multiple patches are indicated. The patches are of no value when the pesticide degrades or vaporizes rapidly or if the patches get wet.

Other examples of environmental sampling including air, soil, and leaf punches. Air sampling is important with highly volatile pesticides. Soil and leaf punches are used for re-entry studies.

Indirect Methods (Biologic Indices)

The indirect method is an alternative research strategy used to measure pesticide worker exposure. This method measures the amount of the material stored in the body or excreted by the body or relates exposure to predictable biologic effect such as cholinesterase inhibition. Indirect approaches, therefore, measure exposure through biologic indices.

Biologic indices of exposure provide important information on acute human pesticide exposures and can sometimes facilitate cause and effect interpretations of suspect or alleged pesticide illnesses of recent onset. The types of laboratory analyses which provide biologic indices of exposure and their toxicological and epidemiologic uses are shown on (Table 10-1).

Table 10-1. Biologic Indices of Pesticide Exposure

Types	Uses
Cholinesterase determination	Verification of Cholinergic Illnesses and Monitoring of the Worker's Exposure to Organophosphate Pesticides
Skin and Hair Residues	Verification of Exposures to Trace Metals (Hg., Arsenic)
Urinary Metabolites (Alkyl Phosphate and Phenols)	Verification of Exposure to the Organophosphate and Carbamate Insecticides and Confirmation of Acute, Chronic, and Incidental Exposures
Adipose and Serum Pesticide	Verification of Acute, Chronic and Incidental Exposures ot the Organochlorine Pesticides Verification of Acute and Chronic Exposures to certain Lipophilic Organophosphate Pesticides.

Since the types and uses of adipose and serum residues are discussed in more detail in Chapter 11 on Pesticide Monitoring and since trace metal toxicologies are not reviewed in this book, only the clinical toxicologic and epidemiologic potential of cholinesterase determinations and urinary pesticide metabolites will be discussed in more detail.

Cholinesterase Surveillance

Workers occupationally exposed to the more toxic organophosphate pesticides should be offered an initial pre-employment cholinesterase determination followed by subsequent cholinesterase testing on a regular basis (usually monthly). The laboratory method should be one that provides both red blood cell and plasma values. RBC values are more informative of exposure than are plasma and worker should be withdrawn from exposure when exhibiting greater than 50% inhibition.

Red blood cell and plasma cholinesterase determinations have been the traditional exposure instruments for measuring organophosphate exposure. The different laboratory methods are discussed in Chapter 9 and the clinical interpretations of enzyme levels are discussed in the section on organophosphate and carbamate systemic poisoning (Chapter 8).

Urinary Pesticide Metabolites

In addition to blood, pesticide metabolite studies in urine offer an alternative mechanism for exposure assessment. The multiresidue procedure particularly with the more recently developed analytical modifications, provides a fairly reliable method for assessment of all routes of exposure.

Urinary Metabolites and the Confirmation of Pesticide Poisonings

The alkyl phosphate and phenolic urinary metabolites together provide highly specific clinical and toxicological evidence of chemical exposure. As will be seen from case examples presented later, both are excreted rapidly in the urine, and are indicative of recent exposure. The major urinary alkylphosphate metabolites which can be identified following human exposure to organophosphate insecticides are: DMTP (dimethylthiophosphate), DMP (dimethylphosphate), DETP (diethylthiophosphate) and DEP (diethylphosphate) (Shafik et al. 1973a). For malathion, for monitoring purposes, the mono-acid and di-acid metabolites are the major urinary metabolites, and are superior to the alkylphosphates which are the minor metabolites (Shafik & Bradway, 1971).

In addition to the urinary alkylphosphate metabolites, some organophosphate insecticides have phenolic metabolites as well (Shafik et al. 1973b). Thus, with ethyl parathion, paranitrophenol is excreted together with DETP and DEP; and with chlorpyrifos (Dursban®), 3,5,6-trichloropyridinol is excreted in addition to DEP and DETP. The various alkylphosphate, phenol and other types of urinary metabolites where reproducible laboratory methods are available for exposure assessment studies are presented in Chapter 9, Tables 9,1-5.

Some methodological problems still exist particularly with low level alkylphosphate concentrations, but surveillance of the worker through urine testing is more acceptable than is surveillance by repeated veni-puncture.

The collection of a 24-hour urine specimen is the most accurate way to determine total worker exposure, but practicality favors the use of timed urine collections; concentration differences are avoided by correcting to creatinine levels with the metabolite being expressed ug/mg of creatinine.

Collection of Biologic Samples for Exposure Assessment by Biologic Indices

Successful chemical verification of pesticide exposure is extremely dependent upon the quality of the biologic sample(s) submitted for analyses. The attending physician and staff are responsible for the proper collection of blood, vomitus (or gastric lavage) and urine. If subsequent blood and/or urine samples are to be collected, the scheduling should be done as soon as possible after consultation between the physician and the toxicology laboratory has taken place.

The general rule to follow when collecting samples is:

1. Obtain 10 cc of blood in a heparinized glass tube (for cholinesterase), and

2. Collect another 10 cc in a plain glass tube (intact pesticides) and

3. For urine and/or vomitus or gastric lavage collect 20 cc in a hexane washed glass jar with aluminum foil placed under the cap.

Obtain pre and post 2-PAM bloods. Collect the initial urinary void and any other voids recommended by the physician. Do not combine the voids. If a catheter is being used, isolate the collection every four hours, noting the date and time interval over which the collection was made. If at all possible, obtain the vessel which contained the pesticide and submit it to the laboratory WITH CAUTION! If the vessel is not obtainable, try to collect a few milliliters of the material believed to be the poisoning agent, again with caution. Finally, obtain as complete and accurate a patient's health and exposure history as possible under the circumstances. Submit a copy of the history to the toxicology laboratory.

Each specimen submitted to the toxicology laboratory must be clearly and indelibly labeled with at least the following information:

Name of Patient   Age of Patient

Date poisoning occurred

Time poisoning occurred and time sample collected.

On a separate sheet, give the name of the attending physician and telephone to be used to call back the laboratory results with some history contained.

Another general rule regarding samples is: Keep all samples as cool as possible; freeze all except <u>whole blood</u> whenever possible.

The various environmental and biological indices of pesticide exposures described have great clinical and epidemiologic potential because they provide verified quantitative information on pesticide exposure. The data will:

1. Assist in the surveillance of the worker.
2. Confirm pesticide poisonings.

3. Clarify the duration of pesticide exposures.

4. Confirm who is really exposed and who is not.

5. Validate the efficacy of exposure reduction strategies such as the wearing of protective clothing.

Clinical Uses of Pesticide Exposure Instruments

From a clinical point of view, determinations of the cholinesterase level as a biological instrument of organophosphate and carbamate exposure with which the practicing physician is familiar. Most frequently, these enzyme levels are used to confirm poisoning or for the surveillance of the workers' occupational exposure to the more toxic organophosphate and carbamate insecticides.

In contrast, because of the few laboratories that have the analytical capability to do pesticide residue analyses and urinary metabolite studies, the physician is less familiar with the diagnostic and toxicologic potential of urinary metabolites and levels of intact pesticide in the blood. Monitoring of these breakdown products during the course of a protracted poisoning will often provide useful information as to the level of intoxication and the future therapeutic needs i.e., paraquat levels of 2.0, 0.6, 0.3 and 0.16 mg per liter in 4, 6, 10, 16 and 24 hours survived. We have seen how significant is the initial plasma concentration of paraquat with regard to the ultimate prognosis; monitoring of blood or urine levels during this protracted intoxication provides management information and the same is true for some organophosphate intoxications. Most organophosphate and carbamate intoxications are short-lived and the whole episode is over within a few days. Figures 10-1, 10-2, and 10-3 illustrate this point of

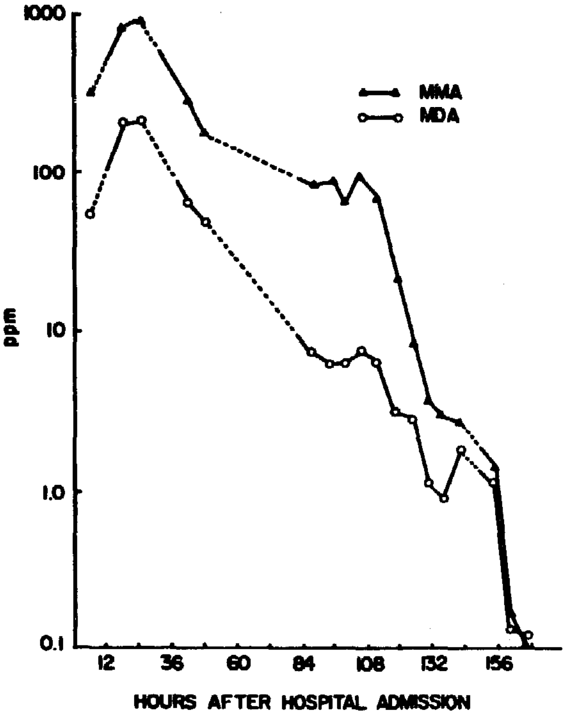

Figure 10-1.
Sequential excretion of malathion mono-acid (MMA) and malathion di-acid (MDA) urinary metabolites following oral ingestion of 50% malathion concentrate.

view for they provide initial and subsequent excretions of urinary metabolites from a malathion intoxication, a chloropyrifos intoxication in a 3-1/2 y/o child and in an occupational exposure in a 39 y/o male spraying mevinphos.

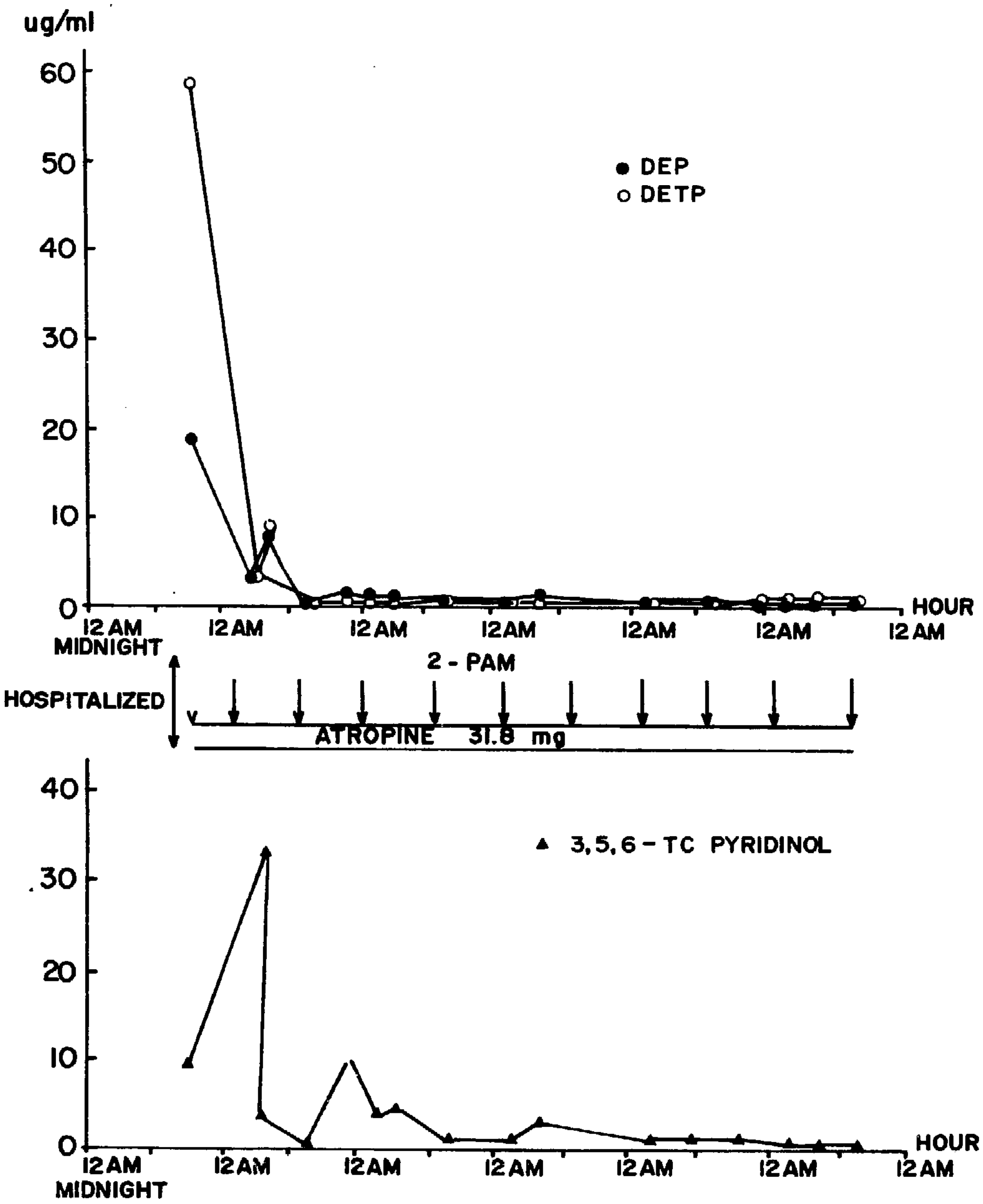

Figure 10-2. *Sequential urinary excretion of alkylphosphate and phenolic metabolites in a 3-year-old black female following ingestion of chlorpyrifos.*

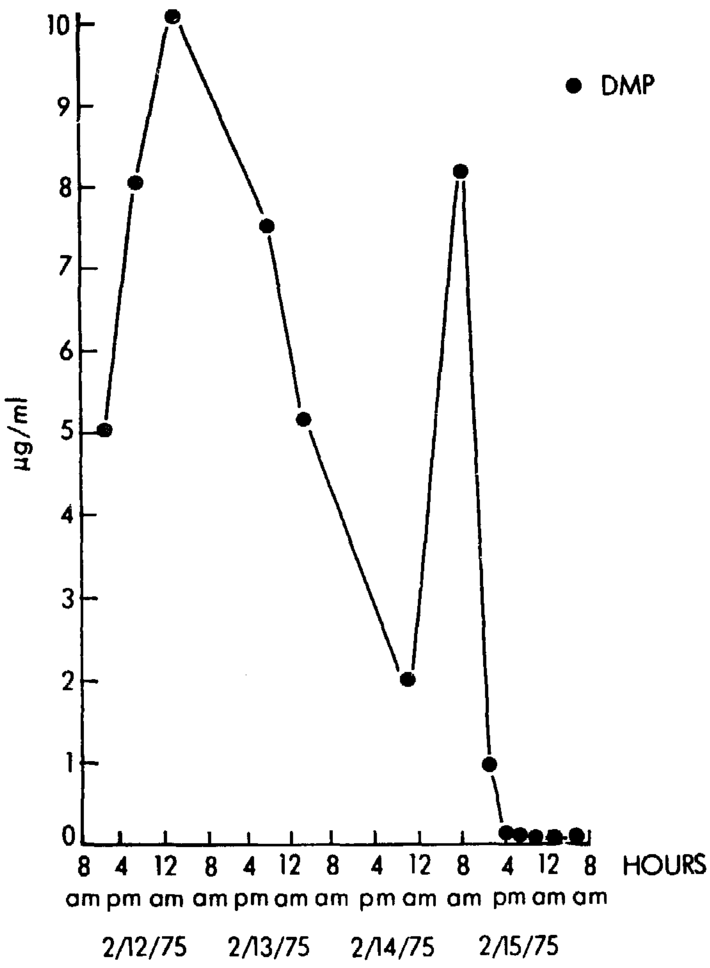

Figure 10-3.

Sequential DMP excretion (ug/ml) in a case of occupational mevinphos poisoning in a 39-year-old black male.

The sequential excretions of urinary metabolites shown in Figure 10-3 are typical of the excretion profiles of organophosphate poisonings which are of short duration; for this mevinphos intoxication the whole episode was over within 32 hours.

This is not however always the case for some lipophilics have a high octanol partition coefficient; the cholinesterase changes, the blood and adipose levels of a dichlofenthion case are shown in Figure 10-4 (Davies, 1975).

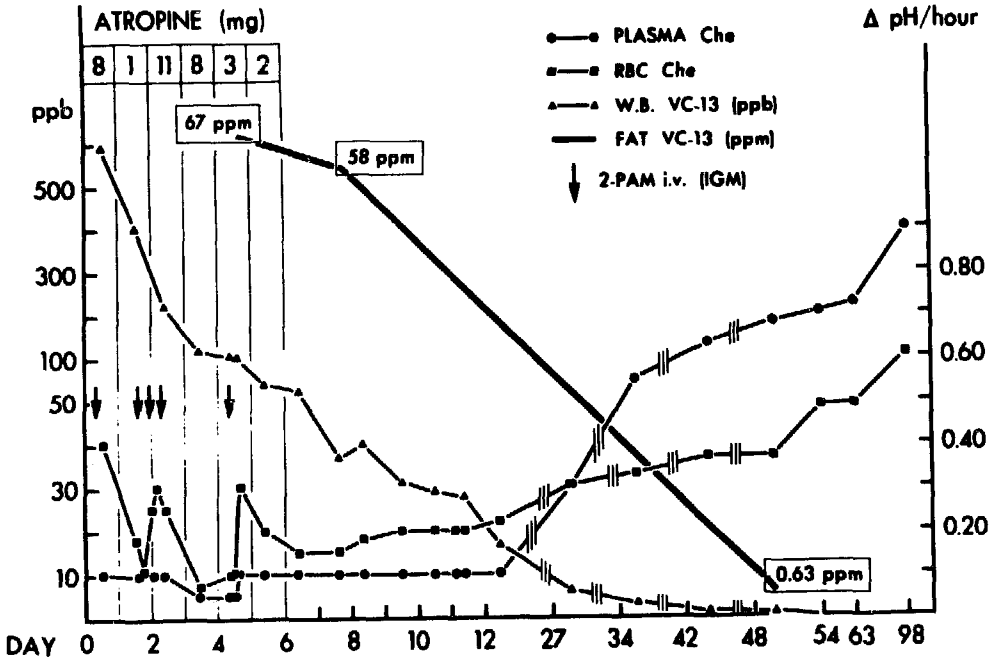

Figure 10-4. *Chronic organophosphate poisoning by a lipophilic pesticide. Clinical and residue findings in dichlofenthion intoxication.*

Verification of Exposure: Who is Really Exposed and Who is Not

There are times when the histories of work exposure, given by the worker, have not been corroborated by the exposure data and both metabolite and/or air sampling studies of pesticide residues have provided unexpected findings. For example, recent studies of EDB inhalation exposure during a citrus fumigation were examined. The dose of EDB among operators (both inside and outside the formulating plant) ranged from 2.3 - 7.5 ug/kg/per year. Workers in the warehouse had mean levels of 282 ug/kg/per year. However, a stickman who simply unloaded citrus cartons into the warehouse had an exposure of 152/ug/kg/per year.

Findings such as these emphasize the importance of exposure assessment for the protection of the occupationally exposed workers.

Epidemiologic Use of Pesticide Exposure

For the most part the biologic exposure instruments are reflective of recent exposure, therefore, have little exposure potential for long-term studies of disease. In these circumstances, measurement of the degrees of pesticide exposure are dependent upon the nature of the pesticide work being done. Great variability exists between the job categories and exposures are usually multiple. In Florida, based on observations and exposure assessment studies, the pesticide mixer/loader is the person most heavily exposed in the field. Based on data compiled from records for the California Department of Public Health ground applicators were heavily exposed, gardeners were next, indoor warehouse workers were third and mixer/loaders were fourth. In this State where closed transfer systems are essential and required the least exposed occupational group were aerial spray and mosquito abatement applicators (Kilgore and Akesson, 1980).

The use of these biologic indices are especially valuable from an epidemiologic point of view when they were used to evaluate pesticide exposure and ways in which this can be reduced. Intervention epidemiologic studies are particularly useful in evaluating pesticides exposures and ways in which this can be done. This was borne out by a design to measure the intervention potential of protective clothing. The reduction of exposure through the wearing of protective clothing is a good example. Here the urinary metabolites could be used, the exposure of workers is measured by quantifying metabolite excretion and re-examination of the workers after they wear protective clothing.

Great strides have been made by technical advances in pesticide formulation and innovative mixing and loading devices. Insufficient attention has been given to the reduction of exposure which can be effected by the wearing of adequately laundered clothing which is comfortable and acceptable to the worker when working in hot and humid areas. Laboratory studies on different fabrics have suggested that 100% cotton fabric was effective not only in reducing penetration but, when pretreated with fluoroaliphatic carbon resin, enhanced the repellency of the material against accidental spillage.

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Chapter 11

Pesticide Monitoring and Human Concerns

Davies, J.E. and Freed, V.H.

Shrimp Boats at Tjeribon

SUMMARY

The bottom line of all monitoring programs is to protect the health and welfare of man and the environment. At present the major thrust of pesticide monitoring programs is food analysis which is concerned with the compliance of regulations. Existing human monitoring data indicates that there is an urgent need in the future to better harmonize food monitoring programs with existing human tissue and environmental monitoring programs.

INTRODUCTION

In the interest of protecting both the environment and human health, pesticide monitoring is an essential ingredient of safe pesticide management. It is now readily apparent that widescale manufacture and use of pesticides as well as other chemicals results in exposure of man or contamination of food and environment. It is essential that we know whether the presence of such chemicals may reduce the productivity of our land or cause problems of human health. The way in which we obtain such information is to "monitor" or analyze crops, food, soil, water and man himself. It is only by doing this that we can avoid a potential disaster.

PART I - ENVIRONMENTAL PESTICIDE MONITORING

From the point of view of environmental monitoring we need to know what chemicals may escape to the environment and at what levels they may be harmful. This leads rather quickly to a realization that until one can identify these compounds with certainty and measure their presence in selected compartments of the environment, effective control of these chemicals is essentially impossible. We will try to show the need for sound use of chemical analysis and monitoring in the evaluation of safety of chemicals to man and his environment.

Analysis consists of the identification of chemical entities and the quantitative measurement of amounts present. For purposes of toxicological evaluation, it is important to know whether the toxic effects of a commercial product are due to the major component or to contaminants that may be present as isomers, by-products or unreacted intermediates. Knowledge of secondary products formed in the environment lies at the other end of the measuring scale. The detection of concentrations over the range of 0.01 ppm (parts per million) to 100 ppm is not unusual in a modern laboratory equipped with readily available instruments. This sensitivity is due largely to the immense reservoir of skill and knowledge.

Monitoring is the process of following a specific chemical through the environment. The selection of the most effective means is not necessarily simple. It requires a wide range of considerations, including for example, toxicity of the chemical which determines the limit of detection required of the analytical method, its behavior in the environment as predicted by chemodynamics and statistical planning.

The ultimate decisions to monitor, what to monitor, how to monitor, when to monitor, and when to stop monitoring, involve the allocation of considerable resources. The quality of planning in a monitoring program will control the utility of information produced and thereby the success of monitoring. The principles that should guide that planning follow.

Types of Environmental Monitoring

The term "monitoring" carries the meaning of measurement of change made over time. One may distinguish at least 4 types of monitoring which differ according to the purpose for which the observations may be gathered. These are:

a. Reconnaissance monitoring involves periodic observations with the objective of determining changes with time, often with the implication that some, perhaps undefined, corrective action may be taken if trends become alarming.

b. Surveillance monitoring, consists of observations which are made periodically to support an enforcement program and to insure compliance with regulations.

c. Subjective monitoring, or spot-checking may be undertaken for a variety of purposes especially, the investigation of an accidental spill or determination of general levels of hazard.

d. Objective monitoring provides data primarily for use in developing and confirming quantitative models and simulation.

It may often be appropriate to start monitoring before the chemical has been released, this monitoring information readily becomes useful only after the chemical has entered the environment.

Monitoring by Chemical and Biologic Techniques

Both direct chemical analysis and measurement of biological response may be applicable to monitoring programs.

Direct chemical measurement may be made of the material in question, or of its recognizable breakdown products, in the physical substrate or in the biota. Data may be gathered on concentrations in the water, the soil, or the air, and in the tissues of animals, plants, or man, in food substances, or in the products of industry.

Beyond the chemical analysis of residues in tissues, monitoring of the biota is useful for determining the nature and the extent of the effects of chemicals on organisms. Chemicals may produce specific physiological responses in individual species. For example, some organochlorine insecticides cause egg shell thinning in certain predator birds, thereby reducing hatching success and threatening reproductive capabilities. Another example is the inhibition of cholinesterase in man and animals following exposure to certain organophosphate chemicals. Appropriate methods for determining the effects of chemicals in the environment are discussed elsewhere in this report.

Once the response of a living organism to a chemical is known, this response can be used in a biologic program as a measure of the concentration of that chemical in the environment. For example, cages of fish placed at intervals in a stream could indicate how rapidly an upstream source of contaminants is being diluted or decontaminated; also plants grown in a filtered air enclosure in the field could indicate by contrast the degree of air pollution.

As a first approximation, the species chosen for monitoring would be the one likely to received the highest exposure to a chemical based on its probable distribution in the environment; however, other factors must be considered in the selection of a species such as its availability, sensitivity, and value to man.

The species should be reasonably available, both currently and in the future, if long-term monitoring is contemplated. The most sensitive species would generally be desired, provided that it is not so uniquely responsive to certain chemicals that erroneous conclusions might result. Conversely choice of highly resistant species may lead to a false sense of security. Species of commercial value to man will, of course, be important, but monitoring should not exclude species of lesser economic value that are good indicators of environment change. Ease of studying and the availability of monitoring methods for particular species must also be considered.

Strategy of Monitoring

The precise character of a monitoring program must be determined by what is known of the properties of the chemicals in question, and the specific objectives of the program. Together, these determine whether monitoring should be done, where, with what materials, how often, with what statistical precision, and how the monitoring effort may best be divided among the several programs of a monitoring system, or among the parts of one monitoring program.

a. When to Monitor

The decision to initiate, continue or terminate a monitoring program is essentially one of balancing the cost of monitoring against the cost of damage to man and the environment if contamination exists and continues undetected. Typically, it will not be made by the persons who carry out the monitoring. It must be an advised policy decision based on the best available technical knowledge which may often be limited, and the best technical advice. Its elements are almost as complex and varied as those involved in the decision to restrict the production or use of a chemical.

Adequate consideration must be given to the consequences of serious exposure and to the likelihood that the chemical will be encountered in the environment at levels requiring corrective action. Therefore, the decision to monitor will rely heavily on the estimate of exposure levels and on the results of tests for effects, both on man and on the living and non-living components of his environment. The estimate of exposure levels should be revised periodically to account for changes in the volume of production, pattern of use, and method of disposal.

The intensity of the monitoring effort should be no greater than that required to detect important changes in the level of contamination in time to permit corrective action. Some materials of low volume and low toxicity may require only infrequent determination because rapid changes in hazard are unlikely. Other materials of high volume or great toxicity potential may require more frequent determination. In establishing the frequency of monitoring, it is often necessary, because of limited resources, to weigh the cost of more frequent monitoring against the possible losses due to failure to detect a change in the level of some other hazardous material. When important changes are not anticipated for some extended period of time, monitoring can be stopped without loss of needed information. Monitoring should not resume until there is evidence of renewed danger.

b. Statistical Sampling in Monitoring

There are two different ways of selecting sample materials for analysis. The first method may be termed selection of an "index." This is by far the more common procedure and perhaps always used from some point of view. Here materials are selected because they are judged to be representative of the universe of interest, with judgment and availability predominating in the selection. In the second method of selection an attempt is made to obtain an unbiased estimate of an average or total value by using methods of probability sampling, or procedures as close as practical to this ideal. The emphasis here is on the avoidance of the well-known bias inherent in judgment sampling. Both kinds of methods of selection may be employed at different levels of the same monitoring program.

Index material is selected because it is practical to obtain, ordinarily at relatively low cost, and may be obtained reliably on a continuing basis. A common criterion is that it must be "representative" or correspond in some usually undefined way to the broader population of interest. In the context of monitoring chemicals in the environment the use of index materials rests upon an assumption that the world can be described by a multi-compartment model (air, soil, water, biota) with ready exchange among all compartments.

The exchange may be either direct or through biomagnification, with the transfer functions being such that the direction of change in one compartment will reveal the direction of change in the whole system. Under these conditions the arbitrary choice of any compartment may be justified solely on the basis of convenience of access. Examples of use of index material are the selection of a single species of fish to represent all fish, or perhaps all aquatic biota, or the use of established stations for the sampling of air.

The second method of sampling is probability sampling. The establishment of unbiased estimates based upon anything reasonably close to probability sampling procedures is practical in only a limited set of monitoring problems. The basic requirement that the probability of selection be known for each item of the sample seems impractical, if not impossible, in most monitoring programs. There are, however, some problems where approximations to this method have been used and others where they could be used more extensively. An example of present use is in the determination of the average pesticide content of various foods in the human diet. An example of potential use is in the determination of average concentration of a chemical in soil, where land could be sampled by area methods.

In studying trends, the use of repeated measurements on the identical primarily sampling units will often increase precision. In some cases the methods of statistical quality control may be adapted for use in monitoring, especially where some defined action is to be taken locally when a trend reaches a certain point. Methods of sequential sampling may increase efficiency of effort in special cases.

PART II - HUMAN MONITORING

History and Goals of Human Monitoring

The small amount of pesticides and their metabolites which, existing in the food, water, air and soil, form part of the modern human environment, are ultimately absorbed and eventually excreted by man. Depending on their physical, chemical properties, these chemical traces may be stored in fat, hair, bone and other tissues of the body for varying lengths of time, or excreted through the regular excretory channels.

Human monitoring programs are designed to implement a continuous observational process of these incidental pesticide exposures.

Ever since DDT was first identified in human fat, several nations recognized the need to document the prevalence of the trace amounts of these fat soluble organochlorine insecticides in the population at large (Wasserman et al., 1967). When trace amounts were identified on a global basis from such disparate regions as the Eskimo in the Arctic (Tatton & Ruzicka, 1967) and the penguin in Antarctica (Durham et al., 1961), the true magnitude of incidental global pollution became more fully recognized, and the international comparisons of these pesticide residues began to appear.

Because food is a major source of human exposure to environmental chemicals of the 20th Century, food monitoring programs are essential for the protection of the health of our society. The ultimate success of these food monitoring programs can only be measured by comprehensive human monitoring programs. The National Human Monitoring Program for Pesticides has such a program and is the mandate of the United States Environmental Protection Agency under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The objective of this program is to monitor on a national scale, the prevalence and levels of exposure to selected pesticides experienced by the general population to be used in risk assessment. The resultant data identifies trends in these exposures and determines the effects of regulatory actions. As was pointed out by Daphne Gloag (1981) human monitoring programs for environmental pollutants should be build into ongoing surveillance of localized "hot spots of environmental pollution."

Human Monitoring Programs

Two main operative programs support these goals, the National Human Adipose Tissue Monitoring Program and the Health and Nutrition Examination Survey (HANES II). Since the fiscal year of 1970, the National Human Adipose Tissue Monitoring Program has been conducted. Adipose tissue is collected from a statistically representative segment of the general population and routinely analyzed for residues of selected organochlorine pesicide related chemicals and polychlorinated biphenyls (PCBs) (Kutz & Strassman, 1975). The Health Services Effects Branch of the Office of Pesticides of the United States Environmental Protection Agency also conducts national surveys. These, as may be inferred, address specific areas of concern not applicable to the general population of the Nation, as a whole, or provide a preliminary evaluation for future monitoring studies under consideration.

Pesticide residue data for selected organochlorine pesticide-related chemicals in human adipose tissue is available from the Fiscal Year 1970 to the present. Since the chemical methodology to detect polychlorinated biphenyls in human adipose tissue was not introduced until later, human monitoring data on this group of industrial pollutants are available from 1972 to the present. The yearly continuity and the population representation design of the National Human Adipose Tissue Monitoring Survey allows trends in human pesticide exposure over time to be identified and evaluated. Similarly, the distribution of pesticide residue levels in subsets of the general population having different demographic (age, sex and race) or geographic characteristics may be assessed. The structure of this annual survey also provides an intrinsic signaling mechanism for the early identification of potential problems. Thus, for example, sudden changes in the distribution and/or residue levels of chemicals monitored can trigger further investigations.

Results of Human Monitoring Programs in the United States

A. Adipose

In the Adipose Tissue Human Monitoring Program lipophilic pesticides and several other chemically related compounds such as PCB's and PBB's, and PCT's have been identified in most of the United States surveys. Thus, in the 1975 survey of the United States population, based upon the analyses of 566 samples, the following fat soluble pesticides were identified with the following frequencies (Table 11-1).

Table 11-1. United States Organochlorine Residues in Adipose Tissue. National Adipose Tissue Monitoring Program, 1975.

Chemical	% Positive	Concentration in ppm, lipid basis Estimated Geometric Mean
Total DDT Equivalent	100	5.16
Hexachlorobenzene	91	0.05
alpha BHC	1	0
beta BHC	97	0.26
gamma BHC	1	0
dieldrin	95	0.17
oxychlordane	96	0.14
trans-Nonochlor	96	0.15

PCB's were identified in 94% of samples

Adapted from F.W. Kutz, 1976 Human Monitoring Program.

Several studies have shown that the Total DDT residues are twice as high in blacks as in whites as will be seen from Figures 11-1.

Clustering by homes and positive correlation of social class has also been demonstrated for Total DDT residues in fat and serum (Davies et al, 1972). Racial differences have also been demonstrated for gamma benzene hexachloride (lindane) whereas no demographic variability has been identified with hexachlorobenzene, alpha BHC, beta BHC, dieldrin and oxychlordane. The latter findings are totally supportive of the hypothesis that these residues get into man primarly from food in contrast to lindane and Total DDT (Kutz et al., 1977).

DDT usage has decreased steadily from 1950 to 1972, so one would expect less amounts of Total DDT in humans to parallel this reduced usage pattern; National Monitoring data substantiated this decline (Kutz, et al., 1975).

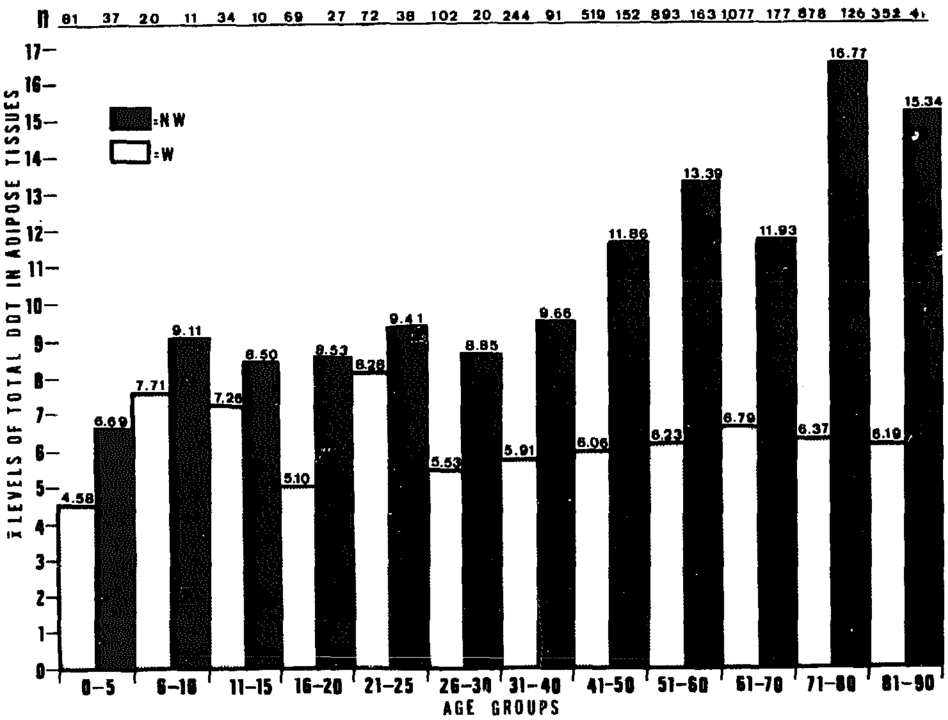

Figure 11-1. *Mean Adipose Levels by Age and Race of Total DDT (ppm) in the General Population from 23 States of the United States, 1968 (Human Monitoring and Florida Data).*

Abstracted from Report of Secretary's Commission on Pesticide, 1969.

B. Serologic

Serological monitoring surveys are also ongoing in the United States. Here under the Toxic Substance Control Act (TSCA), and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the U.S. Environmental Protection Agency (EPA) is mandated to collect data on the exposure of humans and the environment to pesticides and other toxic substances. In partial fulfillment of these mandates, EPA participated in the Second Health and Nutrition Examination Survey (HANES II) conducted by the National Center for Health Statistics of the U.S. Public Health Service.

This national survey conducted between 1976-1980, was an evaluation of the health and nutritional status of the U.S. population. Personal interviews and physical examinations were given to a sample of the U.S. population drawn from 64 collection sites statistically distributed across the continental United States. During the physical examination, blood serum and urine specimens were collected for the EPA. These specimens were then analyzed for selected residues of pesticides, other toxic chemicals and their metabolites.

The Exposure Evaluation Division of the Office of Pesticides and Toxic Substances, within EPA, had responsibility for the chemical analysis and subsequent statistical evaluation of the data. The preliminary summary statistical findings resulting from these chemical analyses of pesticide in human blood serum are shown in Table 11-2.

Table 11-2.

Findings of Selected Chemical Residues in Human Blood Serum (Preliminary Unweighted Findings)[1]

Residue Detected	Origin of Residue	Percentage Quantifiable Positives	Percentage Trace	Highest Value Detected (ppb)[2]	Estimated Geometric Mean[3] (ppb)
trans-Nonachlor	Chlordane and Heptachlor	6.6	64.5	17.0	<1
Heptachlor epoxide		3.9	59.2	22.4	<1
Oxychlordane		3.5	67.6	22.8	<1
Heptachlor		0.5	1.1	3.4	<2
alpha - BHC	Benzene Hexachloride	0.1	1.3	1.7	<1
beta - BHC	Benzene Hexachloride	15.0	45.8	27.8	<1
gamma - BHC	Lindane	0.2	0.6	6.2	<1
delta-BHC	Benzene Hexachloride	0	0	--	--
Aldrin	Aldrin	0	<0.1	Trace	<2
Endrin	Endrin	0	0	--	--
Dieldrin	Aldrin and Dieldrin	9.1	50.4	16.1	<1
Hexachlorobenzene	Hexachlorobenzene	4.4	59.6	16.9	<2
Mirex	Mirex	<0.1	0.1	1.7	<10
o,p' - DDT	DDT	0.4	8.7	42.1	<2
p,p' - DDT		33.3	45.2	80.4	<2
o,p' - DDE		0.4	0.7	3.7	<1
p,p' - DDE		98.7	1.1	378.6	<1
o,p' - DDD		<0.1	0.1	Trace	<2
p,p' - DDD		0	0	11.6	<2
Total DDT Equivalent[4]		98.8	0	447.3	13.9[5]

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[1] Based on the analysis of 3441-4592 specimens collected from the general population via the Health and Nutrition Examination Survey II, National Center for Health Statistics.

[2] Parts per billion.

[3] Where the estimated geometric mean was less than the detection limit of the method, the detection limit was listed.

[4] Total DDT Equivalent = o,p' - DDT + p,p' - DDT + 1.114 (o,p' - DDE + p,p' - DDE + o,p' - DDD + p,p' - DDD).

[5] Percent DDE of Total DDT = 89.4.

Table 11-3.

Findings of Selected Chemical Residues in Human Urine (Preliminary Unweighted Data)[1]

Residue Detected	Origin of Residue	Percentage		Highest Value Detected (ppb)[2]	Estimated Geometric Mean[3] (ppb)
		Quantifiable Positives	Trace		
alpha-Naphthol	Carbaryl Naphthalene	1.9	17.9	4060	<100
Isopropoxyphenol	Propoxur	3.4	10.4	1470	<40
Carbofuranphenol	Carbofuran	3.1	3.7	350	<40
3-Ketocarbofuran		3.2	0.5	1030	<30
Pentachlorophenol	Pentachlorophenol Lindane Hexachlorobenzene	72.2	14.9	2670	3[5]
para-Nitrophenol	Methyl and Ethyl Parathion	2.3	7.7	143	<10
2,4-D	2,4-D	0.3	1.8	212	<30
2,4,5-T	2,4,5-T	ND[4]	<0.1	-	-
Silvex	Silvex	ND	0	-	-
3,5,6-Trichloro-2-pyridinol	Chloropyrifos	5.7	25.3	104	<5
2,4,5-Trichlorophenol	2,4,5-Trichlorophenol Certain Organophosphorous Insecticides	3.3	15.6	56	<5
Dicamba	Dicamba	1.1	5.0	58	<5
alpha-Monocarboxylic Acid	Malathion	1.2	1.8	970	<30
Dicarboxylic Acid		0.5	2.3	280	<30
Dimethyl Phosphate	Any Organophosphorous Insecticide(s)	10.2	32.1	1300	<20
Diethyl Phosphate		6.2	23.6	560	<20
Dimethyl Phosphothionate		5.3	8.3	1810	<20
Diethyl Phosphothionate		5.2	10.3	530	<20
Dimethyl Phosphodithionate		0.3	3.4	170	<20
Diethyl Phosphodithionate		0.1	0.8	390	<20

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[1] Based on the analysis of 6846-6936 specimens collected from the general population via the Health and Nutrition Examination Survey II, National Center for Health Statistics.

[2] Parts per billion.

[3] Where the estimated geometric mean was less than the detection limit of the method, the detection limit was listed.

[4] Not detected.

[5] Detection Limit = 2 ppb.

For more detailed information regarding this survey the reader should contact Dr. Frederick Kutz, at the Office of Toxic Substances, Exposure Evaluation Division (TS-798), U.S. EPA, 401 M Street S.W., Washington, DC 20460 or Area Code (202)-382-3569.

C. Urine

In addition to the lipophilic chemicals, urinary pesticide monitoring studies have also demonstrated widespread but minimal general population exposures (see Table 11-3).

In the U.S., periodic surveys of mother's milk are presently used to ascertain microlevels of lipophilic pesticides.

Data does not presently exist which can demonstrate whether these subtle and minimal exposures are the result of ingested residues of these particular types of chemicals or whether they stem from the domestic use of such pesticides within the home setting. This data gap is one which is in urgent need of investigation and interpretation in order to better evaluate human monitoring programs for residues of organophosphate and carbamate insecticides.

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Chapter 12

Worker Protection

Freed, V.H.

SUMMARY

The manufacture, handling and use of chemicals almost inevitably lead to some exposure. Relatively simple procedures, if followed, can afford considerable protection to the worker. Thus comfortable protective clothing and masks coupled with personal hygiene can reduce the likelihood of serious poisoning. Ordinary clothing can be made somewhat repellent to chemical without loss of comfort. Techniques of application can also reduce exposure levels. Training of workers results in not only greater safety but also more effective workers.

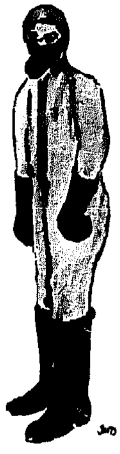
INTRODUCTION

Handling and application of pesticides in other than closed systems almost inevitably results in exposure of the worker (Freed, et al., 1980; Gunther, et al., 1980; Tordior and Van Heemstra, 1980). This is particularly true of the individual applying chemicals with a knapsack sprayer (Lavy, et al., 1980; Wolfe, et al., 1967; Tordior and Van Heemstra, 1980). Attendant with the exposure is the possibility of intoxication resulting in morbidity and mortality. Recent studies have shown that exposure is greatest for those applying chemicals with knapsack sprayers as compared to ground machine application and aerial application (Lavy, et al., 1980). The level of exposure can be minimized, however, through choice of proper formulations of chemical, correct use of the equipment and the use of protective clothing (Doc PB377, 1980; WHO 513, 1973; Finley, et al., 1979; Gunther, et al., 1980).

A number of studies beginning shortly after 1945 addressed the route of exposure experienced by pesticide workers particularly from organic pesticides (Wolfe, et al., 1967). While both dermal and respiratory routes are possible, it was found that the principal route of exposure is dermal with the respiratory route generally many fold less. Dermal exposure cannot be equated with intoxication since the amount of chemical absorbed varies with the chemical, the carrier and the portion of the body surface exposed. However, prudence would indicate that appropriate protection against this exposure is highly desirable. Accordingly, attention has been given in many studies of worker exposure to the role of clothing that might afford such protection (Freed, et al., 1980; Tordior and Van Heemstra, 1980). Although normal work clothing can provide some protection assuming it covers a major portion of the body, several workers have found that clothing may itself become contaminated and afford continuing exposure.

TYPES OF CLOTHING

Rubberized or plastic clothing gives significantly more protection than the usual textiles and has been used extensively for protective clothing (Weeks and McLeod, 1980). However, even in this case, some permeation may occur. Rubberized or plastic clothing though substantially better in reducing dermal exposure, may in hot climates be quite uncomfortable (Freed, et al., 1980) As a consequence, workers object to wearing such clothing thus suffering a higher dermal exposure. Recently lightweight, disposable plastic suits, reported to be much more comfortable, have been developed (Gunther, et al., 1980).



Worker in protective clothing

Since affording protection from dermal exposure is a problem, and rubberized or plastic suits uncomfortable, it is possible to treat ordinary textile clothing with chemicals to increase the repellency of textiles toward spray, thus reducing dermal exposure. Almost any kind of clothing made can be treated with resin, including leather shoes. It has been found that such clothing may be laundered two or three times before requiring re-treatment.

FORMULATION AND EXPOSURE

As noted earlier, whether or not ill effects result from exposure is dependent upon the dosage received. If precautions are taken to select the correct formulation for minimum exposure hazard, proper application procedures followed and protective clothing worn, the exposure may be reduced. Apropos of formulations it should be noted that wettable powders usually afford both less dermal exposure and absorption than do emulsifiable concentrates. This is explained on the basis that the chemical is sorbed onto a clay or other carrier to form the wettable powder. The clay, or the carrier, being particulate and sorptive in character less readily remains on the skin and also reduces the rate of entry (Doc PB377, 1980; WHO 513, 1973).

MIXING, LOADING, APPLICATION

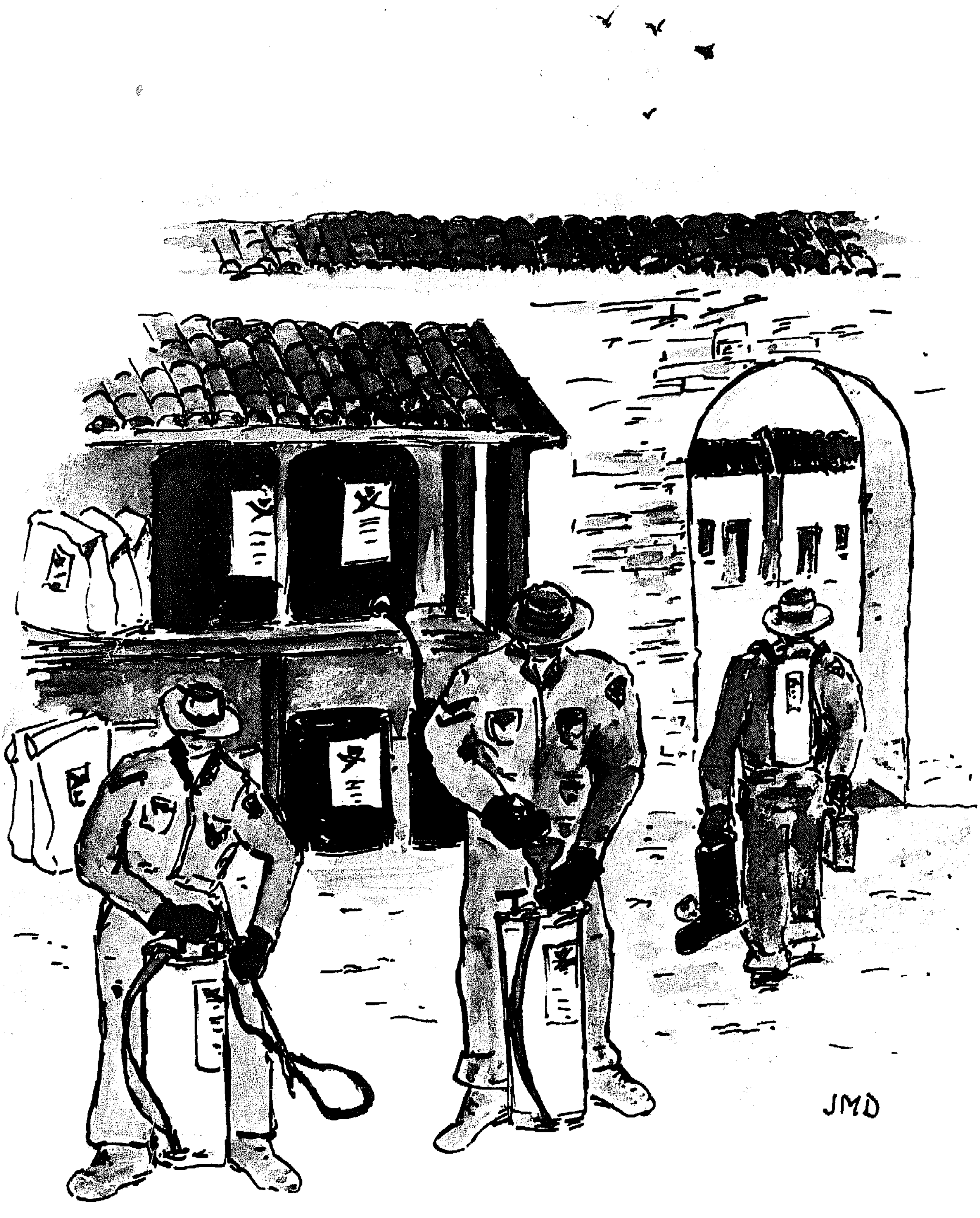
Whatever formulation is being used, the exposure will come during the handling, mixing and application of the spray itself. Assuming that due precautions are taken to avoid exposure during the handling and mixing, what then can be done to reduce exposure during application? Again, assume that the application is being made by the small farmer utilizing a back sack sprayer. Much of the exposure will come from the very fine spray mist, particularly if being applied at low volume and relatively high pressure. In contrast, the exposure to these small droplets can be minimized through the use of coarser nozzles and larger volumes of water (Lavy, et al., 1980; Wolfe, et al., 1967). Another important means of exposure in the use of a back sack sprayer comes from the plants themselves (Finley, et al., 1979). The tendency is for the operator to hold the spray nozzle in front so that they can better see to make the application. This wets the plants in front of them and as they walk through the sprayed area, the spray deposit on the plant wets the trouser legs or gets directly on the skin, resulting in dermal exposure.

If instead of holding the spray nozzle immediately in front of them, they were to hold it to one side and walk in the unsprayed area, most of this exposure would be reduced.

CONTAMINATED CLOTHING

As the foregoing illustrates, one of the problems is contamination of the clothing with the possibility of subsequent and continuing exposure if that clothing is worn. It is recommended that clothing worn while applying chemicals be removed and laundered daily (Finley, et al., 1979; Freed, et al., 1980).

Since sunlight, particularly the shorter wavelengths of sunlight, decompose chemicals, the clothing should be dried in full sunlight to take advantage of this decomposition.



Mixing Chemicals

WHEN PIPED WATER IS AVAILABLE

PLACE SOILED CLOTHING IN A SEPARATE HAMPER

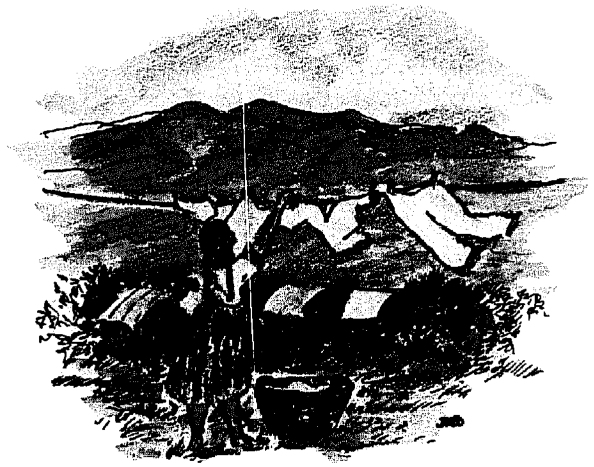
SHOWER IN RUNNING WATER

WASH PESTICIDE CONTAMINATED CLOTHING SEPARATELY

WHEN PIPED WATER IS NOT AVAILABLE DO NOT WASH IN RIVER

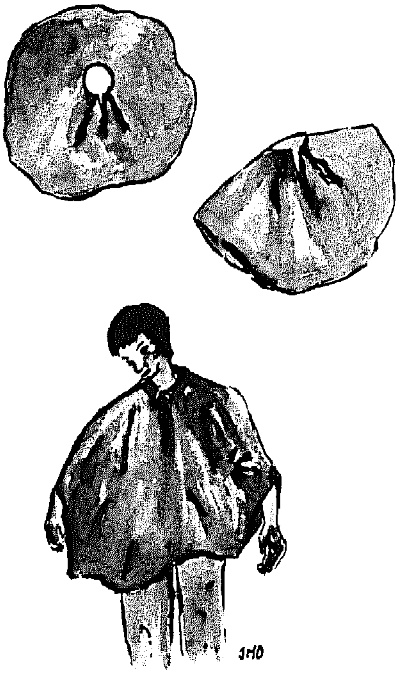
BATHE IN A BOWL OF WATER

WASH CLOTHES IN A TUB



DRY IN SUNSHINE AND WIND

In fact, if clothing is heavily contaminated by chemicals, it may be desirable to spread them out in full sunlight for a day prior to laundering them. This reduces the likelihood of familial contamination or, as might be the case, where the clothing is washed in the stream, contamination of water.



Garment Affording Protection
Poncho

Where it is not always possible to launder clothing worn during spray application daily, some protection can be afforded by an additional item of clothing to be worn. In this instance a large piece of cloth cut to form a "poncho" that drapes over the body can be helpful. This particular item of clothing would be especially useful to the person using a knapsack sprayer, especially if the cloth were treated with the fluoroaliphatic resin (Scotchgard®). This would prevent the individual using the sprayer from spillage or leakage of the sprayer as it was being carried. To make such an item of clothing, a large piece of cloth with a hole just large enough to slip over the head cut into the center and then draped over the body and perhaps tied around the waist. The cloth should be large enough such that it covers the body to about the knees. Even better would be a large slip-over smock with long sleeves and buttons at the neck. A backing flap at the neck would avoid exposure if the head opening were left unbuttoned. Again, it should be noted that treatment with resin (Scotchgard®) is desirable.

RESPIRATORY EXPOSURE

Face Mask

With the temperatures normally encountered in tropical and subtropical regions, respiratory exposure can be a problem due to vaporization of the chemical and of course, to the small aerosol droplets that be formed. If nothing better is available, a clean rag tied over the mouth and nose will reduce the amount of respiratory exposure. For more highly toxic materials, however, the rubber face mask should be used. These, of course, are uncomfortable and difficult to get workers to wear. More recently, research is being undertaken to develop a very light cloth face mask that would adsorb vapors as well as protect against aerosol droplets. This would be reasonably cool and comfortable, not unlike a bandana worn around the face. While the preliminary results with this device look promising, more research is needed before it can be recommended.

HANDLING CONCENTRATE OF CHEMICALS

Studies have shown, not unexpectedly, that those who work or handle the concentrated chemicals received a much larger exposure than those working with the diluted product (Gunther, et al., 1980; Lavy, et al., 1980; Tordior, and Van Heemstra, 1980). Workers in manufacturing and formulating plants, those who mix the chemicals, or are loading the chemicals into a sprayer, whether a backpack sprayer, mechanical ground applicators, or airplanes, stand a risk of greater exposure. When handling the concentrate, extra precautions in the way of protecting clothing, good ventilation, and availability of equipment and supplies to deal with spills should be observed. For example, in the manufacturing or formulating plant operations with a chemical, if not a closed system, should be on a level surface with no obstructions to cause accidents by stumbling or jostling of the individual as he handles the chemical. The area should be well lighted and have a positive airflow. The airflow should be away from the operator carrying the fumes or dusts into the proper ventilation and filter system. Where large quantities of concentrate are being handled, the floor should be of concrete so that in the event of a spill it can be washed and the contamination removed.

Mix with wind to carry chemicals away

Further, when working with chemical inside a building, the access to doors should be clearly marked, and no barrier placed in the route of escape. It is advisable also not to work alone if the chemical is particularly hazardous.

In dealing with concentrated materials outdoors, the appropriate protective clothing is still required; such clothing should include glasses or a face shield to avoid splashing into the eyes. The individual should always work with the chemical with the wind carrying it away from the worker. The mixing and handling should be well removed from any water supply system, or any area where children or animals might have access.

A need for observing safe practice in the handling, particularly of concentrated materials, cannot be overemphasized (Document PB377, 1980; WHO 513, 1973). Observing the correct procedures, wearing protective clothing, and handling the material in designated areas will go a long way in avoiding untoward accidents. Also, the more knowledgeable the workers are of correct procedures, and the nature of the material being handled, the more likely they are to follow these procedures.

TRAINING

While what has been said before tells one how to reduce the likelihood of exposure and hence toxic effect of chemicals; unless this is known by the operator he is unlikely to take advantage of such practices. It is therefore important that in order to protect the operator, every effort be made to educate him in the proper practices. Such education can come from meetings, individual conversations with appropriate agricultural experts, through special booklets using drawings for illustrations or the use of cheap filmstrips.

Training is the responsibility not only of government and universities, but of the chemical industry, and other industries involved in agriculture. It would be most desirable if government, universities, and industry could all join forces in a common program to help those who handle and use pesticides and how to avoid their adverse effects.

The cost in time and money to train people handling and using chemicals to avoid the hazards is quite small and the investment can pay handsome returns. Not only does this help to prevent the human misery ensuing from poisoning which is the important factor, but it also retains a knowledgeable worker on the job. Clearly, not all workers need the same level of training since the intensity and length of exposure would vary with different types of jobs. The worker in a chemical plant involved in manufacture, formulation, or packaging of concentrates runs the highest risk of being exposed to a large dose or is exposed to the chemical over longer periods of time. In contrast, the individual who works in the field following spraying, though exposed to the residues on the plant for many hours a day, is receiving a smaller daily dose. However, it must be quickly pointed out that with many chemicals the dose or the effect is cumulative so that at even low concentrations long-term exposure has its hazard. All individuals that may come in contact with the chemical as a part of their work should received a certain basic training increasing in direct proportion to the exposure level.

Table 12-1. Why Train Workers?

a. Protection of human health.

b. Increase efficiency of protection.

What sort of training should those handling and applying pesticides receive? These individuals, in order to take the precautions necessary to avoid hazard, should have an understanding of the nature of the chemical with which they are dealing, how they may become exposed, and the steps to take to avoid this exposure. Thus, they should be aware of the hazards of spills of the chemical, being exposed to the fumes and the necessity for immediate washing off of any contamination of the skin. They should recognize also that respiratory exposure is much more likely as the chemical is heated up since the vapor pressure increases. They should appreciate the value of good ventilation in working areas including the use of exhaust fans. Beyond this, their training should emphasize the importance of daily changes of clothing and the necessity for laundering of that clothing to remove contamination. There are instances of record where an individual has been poisoned from just such contaminated clothing (Warren, et al., 1963).

Table 12-2. What Should Worker Know?

a. Basic facts about chemicals.
b. Toxicology and safe handling procedures.
c. Protective clothing.
d. Hygiene and first-aid.
e. Accident response.
f. Use of chemicals.
g. Fundamentals of toxicology.

The question is how should one go about training workers, and perhaps the best method is by example; showing the safety practice to be observed, and then the proper supervision. However, this is not always practical, so we turn to the classroom techniques, the use of illustrated booklets, and a variety of other teaching techniques.

Table 12-3. Training Techniques for Workers.

a. Training sessions prior to employment.
b. Booklets and instruction kits.
c. Film strips.
d. Slide-cassette for self-learning.
e. Special lectures.
f. Demonstrations.

The field worker, though not handling pesticides, may receive exposure through residues on the plant or through drift during the spray operation. Training for field workers, then, should emphasize the need to delay entry to the field for a safe period, avoidance of drift and removal of residues from the body by washing. Additionally, the worker must be apprised of the contamination of clothing and the need for frequent change and laundering.

Table 12-4. Protection

a. Protective clothing.
b. Ventilation.
c. Pollution control.
d. Equipment and supplies for fire and spills.
e. First-aid facilities.

The protection of the worker then consists of both providing adequate training and suitable protective clothing and devices. As the use of pesticides increases, it become more and more important that these two action points be implemented.

In spite of all precautions to ensure worker safety, accidents still happen. Hoses break, spills occur, or someone momentarily forgets the necessary safety procedures. In this case, it is important to be prepared with appropriate first-aid measures to protect the worker.

When an accident occurs, the immediate concern is to remove the worker from the exposure by removing them from the area, or removing the contaminated clothing. This should be done carefully so that the individual assisting the worker does not also become exposed. If the exposure is dermal, as by a splash on the skin, or saturating the clothing, or shoes, the skin should be washed with soap and water immediately, to remove as much of the chemical as possible.

If the exposure is from a splash in the eye, the eye should be thoroughly washed with a stream of water for several minutes to remove as much of the chemical as possible. On the other hand, if some of the chemical has been swallowed, and the individual is conscious, inducing them to vomit will get rid of a great deal of the chemical and reduce the likelihood of more serious poisoning. If the individual is unconscious, however, it may be necessary to have medical personnel flush the stomach to remove the chemical.

Prompt action in reducing the exposure and cleansing of the exposed individual is very helpful, and often may mean the difference of life and death if a particularly hazardous chemical is involved. In any event, it is important to get the victim to medical services where appropriate treatment can be given, together with antidotes that will counteract the poison.

In considering personal safety in the use of pesticides, one should treat all chemicals with great care. This is perhaps the cardinal rule in safety, followed by using the appropriate chemical, applying it in a safe manner, and wearing the necessary protective clothing. Observing these rules, and making sure that clothing is properly decontaminated, will go a long way in avoiding untoward problems in the use of chemicals.

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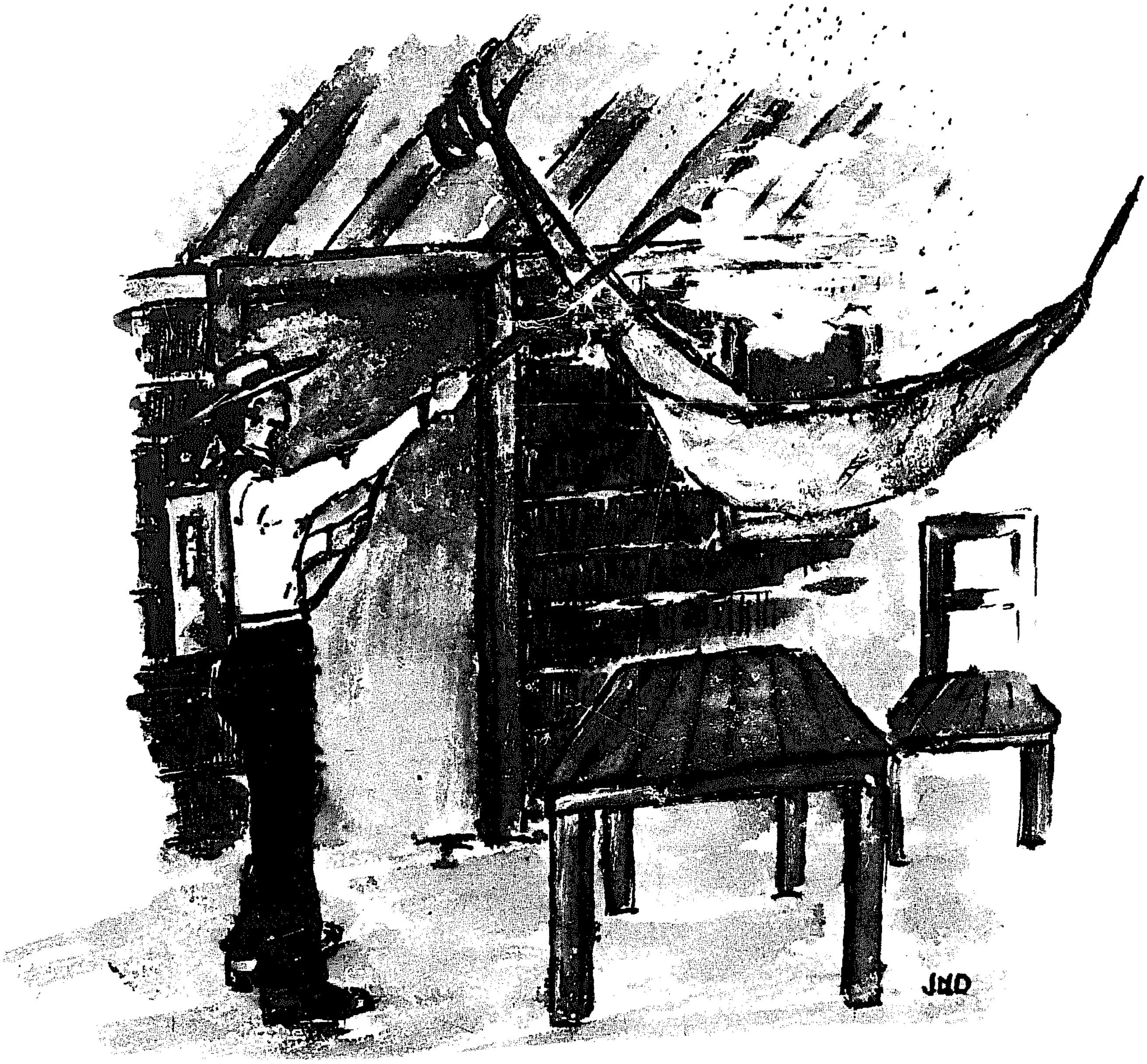
PART III

AGRICULTURE, PUBLIC HEALTH AND ENVIRONMENTAL CONSIDERATIONS

Chapter 13

Application of Pesticides

Freed, V.H. and Fowler Jr., H.W.



SUMMARY

This chapter discusses methods for the effective and safe application of pesticides. Special emphasis is placed on the importance of following the directions on pesticide labels as the foundation for prevention of human poisoning and contamination of the environment. Special comments are also given on selection of the proper chemical and formulation; use of properly designed equipment; and application of chemicals during desirable climatic conditions. Adoption of correct procedures can markedly reduce the hazards from pesticides and ensure attainment of desired results from pesticides without disruption of other husbandry practices.

INTRODUCTION

There are two compelling reasons for proper application of pesticides. First, the material is expensive and improper use is costly. It may either waste material as in the case of over application, or fail to control the pest problem due to poor timing, maldistribution, or inadequate dosage. The second reason arguing for proper and careful application is that these materials are powerful biocides. Improper or careless use of the material can cause human exposure, destruction or injury to beneficial or economically important organisms, or finally, cause unwanted environmental contamination (Green, et al., 1977; Matthews, 1979).

Failure to apply pesticides properly thus may exacerbate one or more of the four basic problems encountered in agromedical management of pesticides. It may result in human exposure, in an unwanted residue, contribute to the development of resistance, or pose a problem of disposal. On the other hand, correct usage and application minimizes the potential for these problems. results in effective pest control, thus achieving desired food production and health protection.

Applying Pesticides

Proper application for safe, effective and economic pest management entails consideration of a number of factors (Coppedge, et al., 1975; Dejonckheere, et al., 1976; Green, et al., 1977; Matthews, 1979). High on the list of important considerations is the selection of the chemical and formulation appropriate for use on the crop and the pest to be controlled. This will take into account not only the effectiveness of the pesticide but also its safety, ease of application, and in some instances, whether or not it will leave a residue that would be undesirable for the succeeding crop. The next item to be evaluated is, what is the best method and timing of application taking into account topography, climate, nearness to bodies of water, protection of humans and desirable organisms, as well as adjacent crops (NAS 1975; Manual of Safe Practice, 1980). Further, the method of application may influence the residual deposit on the treated area on both effectiveness of control and the residue that may persist (Green, et al., 1977; Manual of Safe Practice, 1980). Other factors that enter into devising safe, effective application involves the size of area to be treated, the time available for treatment, the type of carrier--if a spray, and the logistics of getting both the equipment and the chemical to the area to be treated.

This chapter does not purport to be a technical treatise for application techniques so much as it is intended to remind the reader of some of the important points in application and to observe safe procedures aimed at effective pest management. Equipment and chemical manufacturers as well as dealers can provide specific information on the recommended practices for their product. Also, there are numerous technical articles and books that deal with details of equipment and its use in applying pesticides.

FORMULATION AND APPLICATION METHODS

When it has been determined that pest management requires the application of pesticides, one of the first decisions in proper application is to select the chemical and formulation appropriate for the crop, the pest to be controlled, and the area in which it will be used. Safety of the material to humans and the environment, as well as the economics of the use, are two principles that are used in selection of a chemical and its formulation to be applied (Collins, 1974; Green, et al., 1977). The third element of consideration might be that of selecting a chemical different from one that had been used in prior cropping cycles in order to attenuate or slow the development of resistance. Sometimes, it is not possible to observe this latter point because of the limited array of materials available for control of certain species (NAS, 1975).

In selecting a chemical to be applied for a given pest problem, it is desirable to evaluate the chemical and biological properties of the pesticide, the biology of the pest, and the relationship of these elements to the conditions under which the material will be used. A chemical that persists much longer than is required for the control may result in undesirable residues on the crop or in the soil, thus affecting the succeeding crop or becoming an environmental contaminant. On the other hand, if one is attempting to control, let us say, a perennial weed by means of a soil sterilant, a persistence of sufficient length of time to kill the plant is essential. Yet another characteristic of the chemical that may be important is its volatility (Que Hee and Sutherland, 1974). If the chemical is particularly volatile, under warm conditions it may be lost so rapidly as to be a good deal less effective than a chemical of a somewhat less volatility but lower biological activity. It thus becomes of significance in safe, effective pest management, to match the chemical and biological properties of the material to the biology of the organism and the conditions of application. Doing so may permit fewer applications and less of a tendency to over apply.

The equipment for application is largely determined by the formulation chosen, (Matthews, 1979). Thus, with liquids (except fumigants) the common method of application is spraying. On the other hand, the solid formulations such as dusts and granules, require a different equipment for application.

Liquid formulations include a variety of types ranging from soluble materials in solution through emulsifiable concentrates to flowable preparations that may either be finely ground and suspended chemicals or microencapsulated products (Collins, 1974; Dejonckheere, et al., 1976). In addition, there may be a variety of additives that are used to enhance application, improve sticking, or reduce losses after the spray application.

A formulation not a liquid that is applied as a spray is the wettable powder. This, it will be recalled, is a formulation where the active ingredient is deposited on a powder, a wetting and dispersing agent incorporated into it so that the material will suspend in water for spraying.

Granular formulations (see chapter 14) consist of the active ingredient impregnated on granules of appropriate materials. The granules may be of varying size from quite small granules up to the size of a soy bean seed depending on the chemical and how it is to be used. Granular formulations are usually designed for those chemicals that are active through the soil (Coppedge, et al., 1975) or that may be systemic, being picked up by plant roots and translocated to the top. Like dusts, granules can be applied with very elementary hand equipment on up through properly designed mechanical equipment. One of the advantages of the granular material is that the drift during application is minimized as is also, losses due to volatilization of the chemical. Granules are frequently used for band application or for applying in furrows prior to planting. Again, with a given active ingredient, the granular formulation will have a somewhat larger margin of safety with respect to human toxicity than the comparable material made up as a liquid (Manual of Safe Practice, 1980).

Water is a common carrier for spray application but in other instances, particularly with low volume and ultra low volume application of certain insecticides, oil may be the carrier of choice. Spray applications are divided roughly into high volume applications which may be 500 liters or more per hectare, low volume applications that may run more in the range of 50 to 75 liters per hectare, to the ultra low volume application that may be as little as one liter per hectare (Matthews, 1979). A rather specialized liquid application is that of aerosols. Aerosols may be come from the small pressurized containers familiar in household use on to large fog generators often used in mosquito control.

Dust, as indicated in chapter 14 on formulations, are finely ground powders, usually a clay, onto which the pesticide has been deposited. Concentrations of active ingredient may range from 5 percent or less up to as high as 20 to 25 percent. Dusts may be applied quite simply by hand using no more complicated equipment than a cloth, shaker can or hand carried dusters for limited areas, or it may entail, in treating larger areas, mechanical dusters. Dusts, while convenient to handle and require no additional carrier, have certain limitations for broadcast application, First of all, the dusts are relatively more difficult to control in application than a properly formulated spray or granulars. Also, while dusts may make safer an active ingredient so far as human toxicity is concerned, at the same time they result in a somewhat lower biological activity of the active ingredient requiring slightly higher rates of application to achieve the same degree of pest control. On the other hand, dusts are convenient because they are ready to use, may be applied with rather simple apparatus, and have an appeal where a localized treatment is to be made, e.g., a few plants in a garden (Green, et al., 1977; Matthews, 1979).

In the actual application, a number of factors influence the safety and effectiveness of the treatment. There are losses in the use of pesticides in part due to environmental factors and in part due to formulation and method of application that may influence both the safety and effectiveness of a treatent are such things as the carrier and additivies in the formulation, the pressure and type of nozzles used in spraying, and of course, environmental factors such as temperature, wind, relative humidity, and rain fall (Djonckheere, et al., 1976; Green, et al., 1977). Sprays and dusts are more likely to drift in wind than are granules simply because of the differences in the size of the particles. However, in the case of sprays, use of proper size nozzles and as low a pressure as compatible with correct operation of the nozzle will ensure larger drops hence, less drift (Akesson, et al., 1974; Akesson, et al., 1972; Matthews, 1979). With mechanical dusters, equipment has been developed to reduce the problem of drift and dust. In fact, in both sprayers and dusters, electrostatic devices have been incorporated to put a charge on the particle causing them to be attracted to a leaf surface thus ensuring better deposit and less drifting.

It is important, of course, to get the right deposit, particularly where plant surfaces are being treated. Where an insect is relatively sedentary, or in the case of a contact spray for weed control, a thorough coverage is needed. On the other hand, if the material is systemic in its action, deposit of a few large droplets, even though fairly widely scattered, may be equally effective. In order to achieve a more uniform distribution of the deposit, surface active agents may be employed.

A watchful eye should always be kept on the weather. Winds cause pesticide particles to be unevenly distributed and promote drift away from target areas. Generally, it is desirable to make applications when the wind is relatively calm and during the coolest part of the day. This of course is not always possible, and in some instances not applicable. However, it must be remembered that with increased wind there is greater drift and also a faster rate of evaporation of the carrier that further aggravates the drift problem (Matthews, 1979; Que Hee and Sutherland, 1974). In general the following rules are recommended:

1. Ground applications of pesticides should not be made in the presence of winds in excess of 10-15 miles per hour (m.p.h.). [16-24 Km per hour].

2. Aerial applications should be postponed when winds are greater than 6 to 8 m.p.h. [9.6-13 Km per hour].

3. Phenoxy herbicides (e.g. 2,4-D) should never be applied in cross winds blowing in the direction of sensitive non-target plants.

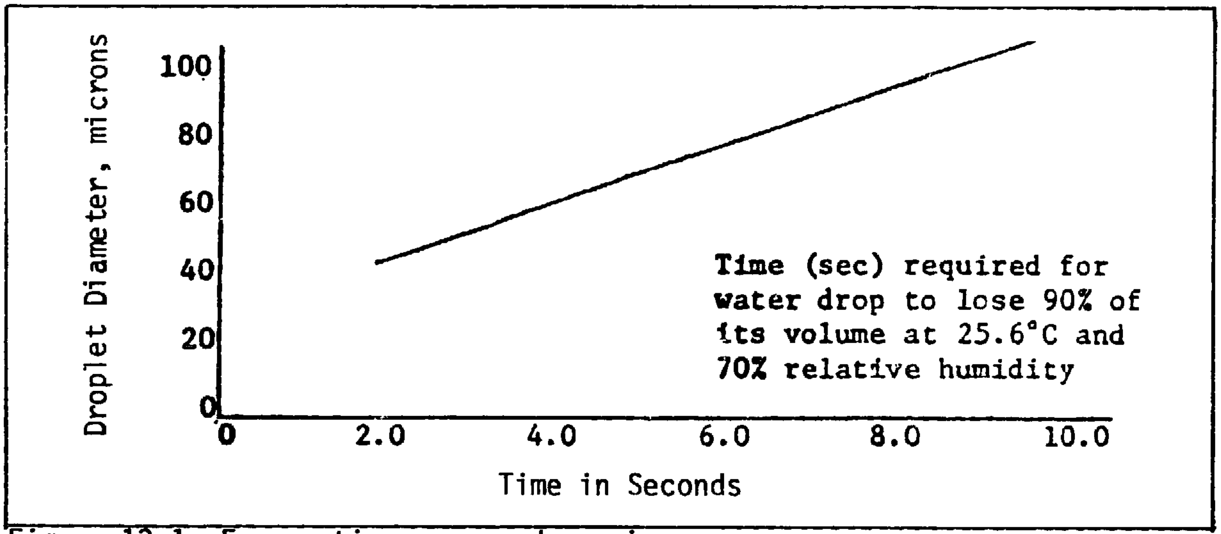
4. Treatment should be postponed if rain is imminent. Rainfall shortly following treatment may significantly reduce the effectiveness of pesticides.

Consider the matter of drift of the pesticide during application. Any of the material not reaching the target area is ineffective and hence waste as well as a potential contaminant of the environment. The drift, of course, is in part due to environmental factors e.g., wind, the application technique, but perhaps to an unappreciated extent may be due to the formulation itself. Particles, particularly spray particles of less than 100 microns diameter, are very likely to drift off the target area even with a very mild wind condition. To some extent, modifications of the volume of application, the carrier, the pressure, and nozzle can control droplet size. However, a factor that may be of some importance is the vaporization of the carrier from the droplet resulting in a droplet of increasing diameter and hence, greater tendency to drift. The problem here then lies not with the chemical itself but with the carrier and the application. What is needed then if one were making an application of a spray under conditions of low relative humidity and high temperature might be an agent in the formulation to ensure maintenance of larger droplet size. Some recent work has revealed a number of agents, notably the polyglycols, that may be effective at relative low concentrations in doing just this.

Table 13-1. Evaporation rate (H_2O, 86°F, 50% relative humidity)

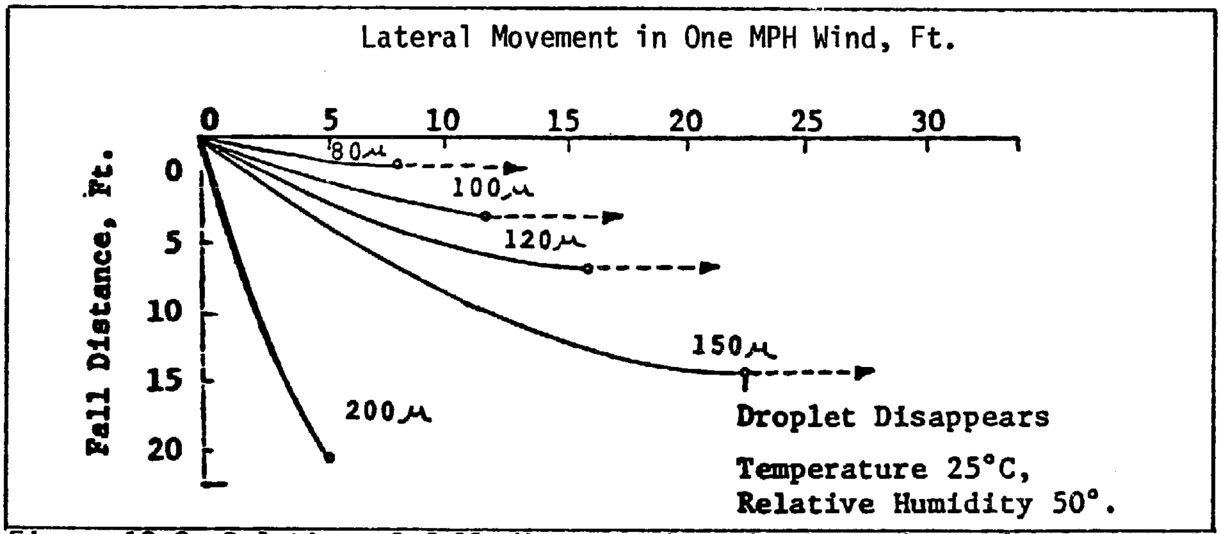
Droplet Diameter in Microns	Lifetime (sec)	Distance of Fall
200	56 sec	69 ft
100	14 sec	6 ft
50	3.5 sec	1.25 ft

To illustrate more fully the problem of evaporation of the carrier, consider the information in Table 13-1 and Figures 13-1 and 13-2.



Time (sec) required for water drop to lose 90% of its volume at 25.6°C and 70% relative humidity

Figure 13-1. Evaporation versus drop size.



Temperature 25°C, Relative Humidity 50°.

Figure 13-2. Relation of fall distance through air to lateral movement for water droplets falling at terminal velocity in a one MPH wind.

Having reached the target which in this case may be the leaf of the plant, the deposit is subjected to photochemical decomposition, vaporization and in many areas wash-off by intense rainfall. Many of the chemicals that we use are particularly susceptible to breakdown by ultraviolet light. We would expect, therefore, that as we go from the northern latitudes toward the tropics, the problem of photochemical decomposition would become greater. The reason for this is the greater proportion of ultraviolet light reaching the earth's surface because of a thinner ozone layer.

Photodegradation of chemicals

We have had no field measurements that tell us precisely how great a problem the photochemical decomposition is as regards chemical persistence, but it does not stretch the imagination to suggest that with some compounds it may be quite important. Therefore, if photochemical decomposition is of particular importance for the specific chemical, it would seem to follow that it would have to be formulated differently to adjust to the varying light conditions. If we have agents to protect human skin from too much ultraviolet radiation, it would then seem possible to develop a formulation containing an agent to protect the pesticide from the radiation.

Loss of chemical deposit through volatilization, particularly within the first few hours of deposit, is probably appreciable (Green, et al., 1977). To illustrate the relative rates of vapor loss of different compounds, Table 13-2 has been compiled. As can be seen from these data, the losses can be quite substantial. These occur during the first few hours following application before the chemical has had an opportunity to absorb on surfaces.

Table 13-2. Evaporation Rates of Chemicals

Compound	P (mm Hg)	Evaporation Loss (g/cm^2-hr)	
		Experimental	Calculated*
Dichlofenthion (20°C)	5.6×10^{-4}	7.8×10^{-7}	2.3×10^{-6}
Fenitrothion (20°C)	2.2×10^{-4}	2.7×10^{-7}	8.7×10^{-7}
Malathion (20°C)	3.4×10^{-4}	5.8×10^{-7}	1.5×10^{-6}
Parathion (20°)	3.8×10^{-5}	1.7×10^{-7}	1.5×10^{-7}
Ronnel (20°)	5.5×10^{-5}	9.2×10^{-8}	2.3×10^{-7}
Methyl dursban (20°C)	3.4×10^{-5}	3.8×10^{-8}	1.5×10^{-7}
Dicapthon (20° C)	3.6×10^{-6}	$\sim 1.5 \times 10^{-8}$	$\sim 1.5 \times 10^{-8}$

*Qcal = $\bar{\beta}$ P(M/2πRT)1/2, where $\bar{\beta}$ is the average evaporation constant and has a value $\bar{\beta}$ = 1.94 x 10-5 (± 11% S.D.); P is the vapor pressure at temperature T (°K).

In some regions, particularly the moist tropical regions, wash-off of a deposit is probably a very important mechanism of loss. The 20 to 25 spray applications often used on cotton in the tropical regions are required to maintain a biologically effective pesticide deposit. In addition to photochemical breakdown and volatilization, substantial losses of the chemical deposit are due to intense rainfall. Just how intense this rainfall can be in tropical regions is illustrated in Table 13-3. With something approaching 12 inches of rain in 24 hours it is not hard to visualize a nearly complete wash-off of a pesticide deposit from the surface of the leaf. If it were possible to design a formulation that would have considerable resistance to wash-off while still retaining its biological effectiveness, there could be a substantial reduction in the number of applications and hence the amount of chemical required for pest control This would not only reduce pesticide loss resulting in greater effectiveness, but would also have the benefit of reducing the incidence of human toxicity and the problem of environmental contamination.

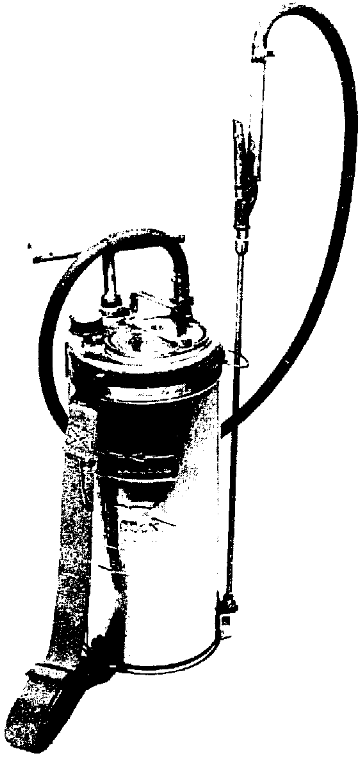
Table 13-3. Rainfall

	Yearly (mm)	24 hrs (mm)
San Salvador	1,778	321 (normal in June)
Concordia, Kansas	644	164 (May)

(World Survey of Climatology, Weather Almanac)

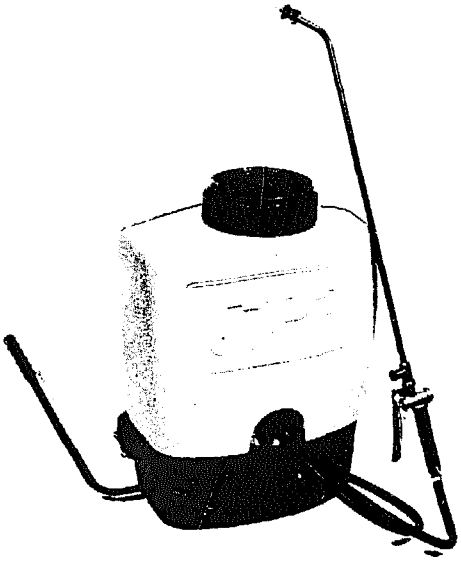
APPLICATION AND EQUIPMENT

There is a great variety of equipment available for application of pesticides (Akesson, et al., 1974; Akesson, et al., 1972; Matthews, 1979). It may range all the way from such simple devices as containers with perforated lids for shaking out a dust or granule through simple hand-held dusters and sprayers to elaborate mechanical equipment for both ground and aerial application. A great deal of pesticide is applied by hand-held or human-carried equipment particularly on small areas or in vector control for public health. The type of equipment available varies from country to country depending on the source of supply or local manufacturers. The following is not intended to be a complete listing of the different types of equipment but merely illustrative of some of the types available.



First to be considered, of course, are those pieces of application equipment that are carried by humans. For application of liquids a variety of hand-held or human-carried sprayers are available. Among them are:

The pump-up sprayer. This type of sprayer has an internal pump used to compress the air to provide the power for spraying. Such a sprayer, carried over the shoulder or back, can be rigged with different types of nozzles or even short booms with three or four nozzles to cover a swath as might be desired in



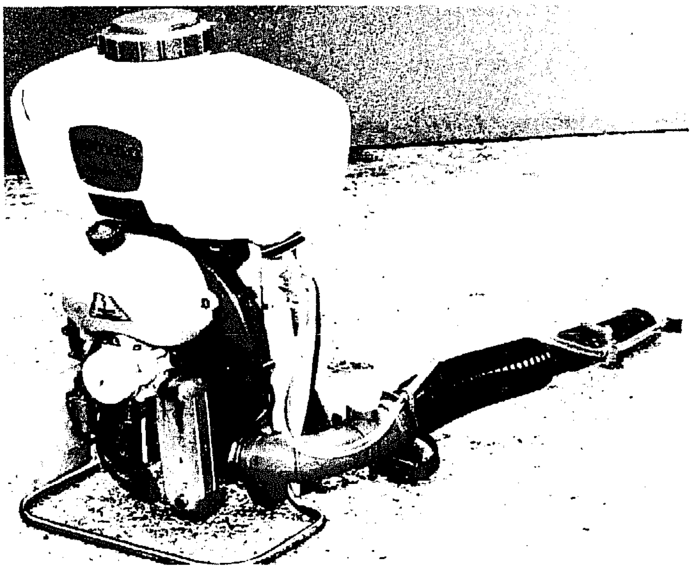
Back pack sprayer

spraying a crop such as rice. It is important with this type of sprayer, as with the next to be described, that the filling hole, hoses, and any pipe or nozzle connection be tight in order to avoid exposure of the operator to the spray mixture.

The back pack sprayer. The back pack sprayer depends on either an internal or external pump, continually operated by hand, for displacement of the spray liquid. It is a widely used type of sprayer since the operator has continuous control of the displacement or spray pressure. As noted above, the equipment needs to be carefully checked to prevent leaks or spillage from openings in order to avoid operator exposure.

Controlled droplet applicators. Controlled droplet applicators are relatively new to the spray scene. Basically, they consist of a rapidly turning disk powered by flashlight batteries. This piece of equipment applies the chemical in a very low volume with the spinning disk giving a quite controlled droplet size. Though requiring a bit more attention to maintain and a continual supply of batteries for operation, these sprayers are becoming very popular in that they give a rather controlled application, require low volumes of carrier and will allow a single individual to treat a fairly large area in a day.

Back carried mist blowers. The back carried mist blower is usually powered with a small, light, gasoline motor and is used in ultra low volume application. Their utility lies in where the pesticide can be applied as a very

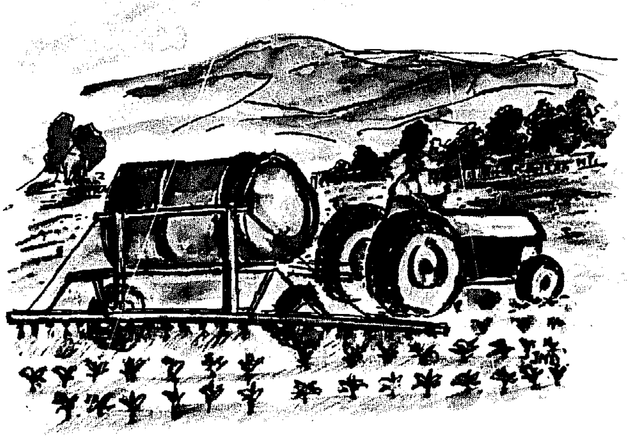


small droplet with the wind generated from the fan driven by the motor, propelling the mist to the target area. The small droplet size ensures a greater uniformity of coverage but also affords a greater problem of drift of the spray. The mist blower is probably used more frequently for application of insecticides and fungicides in vegetative and tree crops than it would be used for application of herbicides.

Wicks and wipes. The wiping of a cloth saturated with a chemical over a weed for controlled application is increasing in popularity. While dipping a cloth into a solution of chemical and wiping it on a plant has been used for years, only in recent times have devices for more systematic application by this method been developed. The devices are usually quite simple with a roller or piece of cloth of the desired width mounted on a hollow tube into which the liquid can be introduced. Perforations in the tube allow the chemical to soak through the cloth where as it is dragged over the plant, comes in contact with the foliage leaving a deposit of the pesticide. Devices such as this have become very popular for treating in between rows of crops with chemicals that might otherwise injure the crop were any spray drift to get on it. The wicks and wipes no only permit selective application with no drift but more, through the controlled application, reduce the amount of chemical that is needed by eliminating wastage.

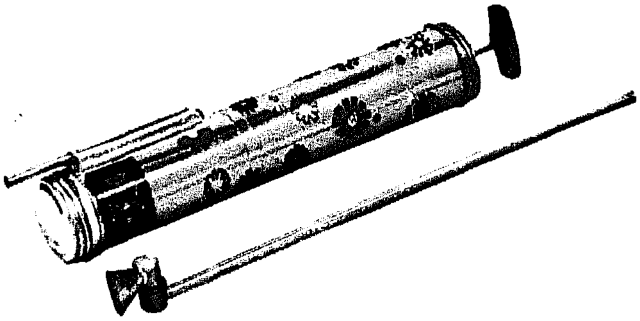
Just as the hand-held or carried equipment comes in a great variety, so does the power-ground machinery for application. The power-ground machinery may range from spray and dust attachments for the very small tractors through the large tractor mounted sprayers to large spray units with the over-sized tires for working in soft or marshy ground. The units may consist of:

Conventional Sprayers. Conventional sprayers consisting of a spray tank and a pump with pressure control and agitation. These may be rigged up with a variety of different nozzles or booms for high, low, or ultra low application (Green, et al., 1977; Matthews, 1979).



Mist Blowers. The tractor drawn mist blower is not unlike the back carried mist blower in that it will have a large fan to provide an air blast for propelling small droplets towards the target area. The mist blower will require a pump to pump the liquid into the air stream where it is then blasted towards the target.

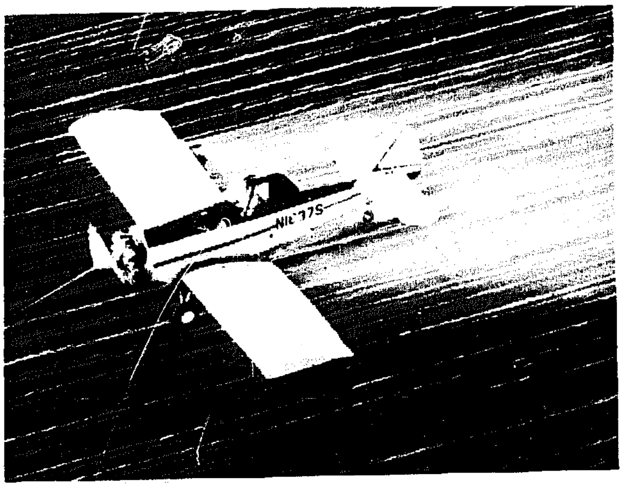
Dusters. The mechanical duster will consist of an especially designed hopper, usually with an auger, to move the dust to the spray nozzle. Again, an air blast is used to propel the dust particle toward the target area. As indicated earlier, some of the modern dusters will have electrostatic devices to give a charge to the dust particle assuring the better deposition.


Hand-held Duster

Granular Applicators. Equipment for application of granules has a similarity to dusters in that they will have a hopper into which the granular material is loaded and then augered out for distribution through predetermined openings. The openings may lead directly into an open furrow in some instances, in others the openings will provide a band application over a row, or it may be for general distribution where broadcast coverage is desired.

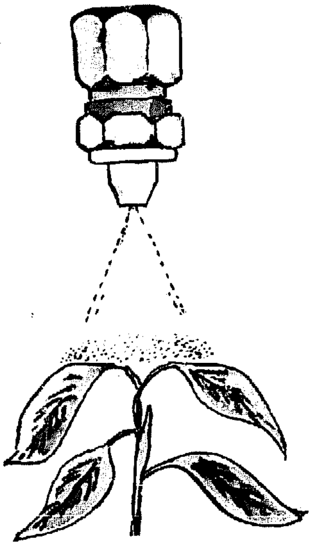
AERIAL APPLICATION

The equipment for aerial application is a specialized field in itself (Akesson, et al., 1974; Akesson, et al., 1972; Matthews, 1979). Two principle types of aircraft are used, namely, the fixed wing and the helicopter. In recent years, manufacturers have built fixed wing aircrafts especially for agricultural applications. In either the fixed wing craft or the helicopter there will be a tank or bin into which the chemical is placed. It is then distributed underneath the craft through some type of boom or distributer for the application. In spray applications the configurations of nozzles and orientation with respect to the air stream, all become important in determining coverage and the potential for drift. The aircraft, either fixed wing or helicopter, may bed used for applying sprays, dusts, granulars, including fertilizer, and can do so at a very rapid rate.

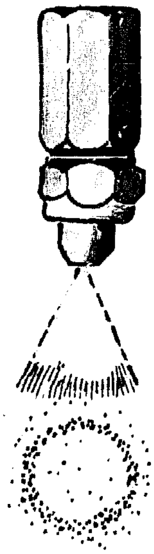


SPRAY NOZZLES

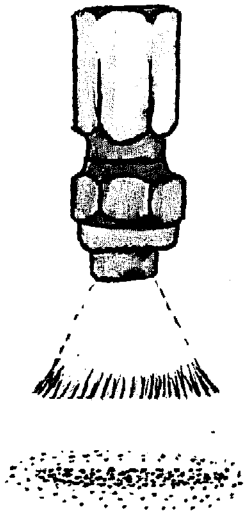
Operators should pay special attention to the nozzles on spray equipment. The nozzle and associated strainers are especially important components for they are controlling factors in the configuration of spray patterns and the rate of spray output at a given pressure. Nozzles come in a variety of types and may be mounted in various ways on spray booms in order to achieve desired results. Nozzles and strainers should be cleaned frequently to ensure that they are operable. The following types of nozzles are commonly in use in both public health and agricultural control programs.



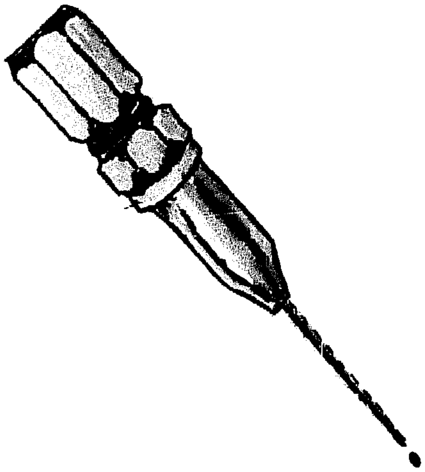
The solid cone nozzle is used by agricultural workers to produce complete coverage of plants in an over-the-top application. Cone nozzles are also used by public health workers for mosquito larviciding and area treatment of vegetation.



The hollow cone nozzle is frequently used for mosquito larviciding and treatment of vegetation for ticks and mites. Cone nozzles with large openings are used for surface spraying of suspensions and other materials. Additionally, cone nozzles are utilized for general pest control in gardens.



Flat fan nozzles are used in agricultural situations for broadcast spraying in an overlapping fashion. They are used in public health programs for application of residual insecticides. Derivations of flat fan nozzles are also used for application of narrow bands. Additionally, another common type of flat fan nozzle is a flooding nozzle for broadcast spraying with a low pressure field sprayer.



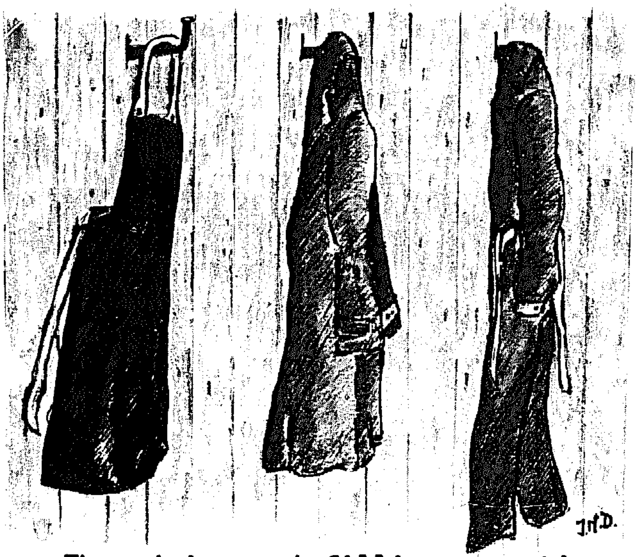
Solid stream nozzles produce a narrow jet spray. This type of nozzle is useful for application of narrow bands of chemicals or injecting pesticides into the soil. Public health workers use this type of nozzle for crack and crevice treatment in houses for control of cockroaches, ants, bed bugs, fleas, etc.

CHECKING AND CALIBRATION OF EQUIPMENT

All equipment to be used in application of pesticides should be carefully checked and calibrated before use. This ensures not only that the proper amount of chemical will be applied but also the checking assures the safety of the equipment in fixing leaks or places where the chemical may splash out. Manufacturers of equipment usually provide detailed information on the current maintenance of all types of equipment and these instructions should be carefully followed as to lubrication, operation, and maintenance of the equipment. Attention should be given to hoses and strainers to ensure that they are working properly and are not leaking. Thorough cleaning of the equipment before use, ensuring that the strainers and filters are clean and operative, may help to avoid having to clean out a plugged nozzle when one is applying a particularly toxic chemical.

Equipment should be calibrated prior to use in order to be assured of applying the correct amount of chemical. In the case of spray equipment, the calibration can be so simple as to measuring the volume of spray liquid, preferably water or whatever carrier is used that is sprayed out in a given length of time. Then, by knowing the volume put out by the nozzle or the boom and the width of the spray path, it is possible to calculate the rate of travel that is required to apply the correct amount of chemical at that volume and pressure desired. With hand equipment it is sometimes desirable to use the carrier, water or whatever it may be, and spray a given area with a particular volume. If the amount of the carrier runs out before the appropriate size area is covered then one knows they are travelling too slow or if there is carrier left after the coverage, the rate of travel is too great. A few attempts like this enables the operator to estimate the proper rate of walking.

MIXING AND FILLING



It is during the mixing and filling operation that exposure to the concentrate frequently occurs. Without protective clothing and adequate precautions, exposure can come about through splashes and spills during this operation. Further, unless the mixing and filling done away from water sources or human habitation, spills may result in bystanders becoming exposed at a later time.

As indicated in an earlier chapter, chemicals should be stored well away from human habitation, animal quarters, and away from water sources. The mixing and filling operations should likewise be carried out away from these places. The mixing and filling should be done out-of-doors. The operator should position himself such that if there is a breeze blowing, it will blow the dust or liquid out away from him. But, even before beginning the mixing and filling operation, the operator should carefully read the label and observe the precautions noted therein.

Where the chemical must be weighed or measured, i.e., the package is not exactly the size required for the equipment used, there should be special scales and measuring devices to be used for this purpose. Transfers should be made carefully so as to avoid spills or splashes that would contaminate the container and the area. Appropriate size plastic jars or containers for such measuring are available and easily cleaned for the next usage. The transfer to the equipment or mixing tank then should be done with the wind blowing away from the operator. Care should be taken to avoid splashes and spills.

The operator should always use appropriate protective clothing including face mask during mixing and loading operations. Protective clothing would include also a pair of gloves, preferably rubber gloves, in the event of a spill of the concentrated mater. (See chapter 12 on worker protection.)

Only after the filling operation is complete and the equipment closed should the mixture be agitated to get uniform mixing.

SAFETY PRACTICES IN APPLYING

The pesticide, as mixed and ready for use, is at a much more dilute concentration but nonetheless, exposure to the spray drift or dust is undesirable. The operator may receive a low exposure at any given time but if he is making application over a period of hours or days, the effect may be cumulative. For that reason, appropriate precautions should be observed.

One of the first precautions that spray applicators should observe is not to apply during periods of high wind (see earlier section). But, beyond this, it is important for the applicator to wear appropriate protective clothing such that the inadvertent exposure is minimized. The type of protective clothing will vary with the chemical being applied and of course the climate. At the very least, the protective clothing should consist of full body covering such as with coveralls, a head covering and some sort of a mask to reduce inhalation of small particles. Nothing else being available, a cloth tied around the face will be helpful but not entirely adequate for all materials.

In making the application, the operator should try, as much as is possible to stay out of any drift of the chemical. This means that even in a slight breeze, spray application should be made so that the wind is blowing away from the operator not toward him. Similarly, in making application with equipment carried by a human such as the back pack sprayer, the operator should not walk through that area that has been sprayed. It is preferable to hold the nozzle to one side and walk in the unsprayed area. The spray deposit on the plants can wet the clothing and soak through to the skin resulting in dermal exposure. By holding the sprayer to one side and walking through the unsprayed area the applicator avoids such exposure.

Finally a word must be said about the problem of plugged nozzles during spray operation. If, by any chance, particulate matter gets into the sprayer it can plug screens and nozzles, necessitating their being cleaned out. This should be done very carefully in order to avoid exposure, with the operator wearing rubber gloves to handle the nozzle. If the nozzle opening itself is plugged, it should be cleaned out with a fine wire rather than the operator putting it to his lips to blow the plug out. Almost anything of the appropriate size, such as a wire or even a sliver of wood, can be used effectively for unplugging nozzles.

CARE OF EQUIPMENT

In closing this chapter it is appropriate to reiterate the importance of proper care and maintenance of equipment for safe and effective pesticide application. Such care and maintenance includes proper cleaning, lubrication, and checking the working parts before attempting to use the equipment (Matthews, 1979; Manual of Safe Practice, 1980). This also involves checking to make sure that all screens and nozzles are clean and in working order, that the pressure regulator is delivering the desired pressure for the applicator, checking the volume output and making sure that there are no leaking connections. When the spray job is completed, the equipment should be drained, thoroughly cleaned and allowed to dry to avoid rust and corrosion of metal parts. Manufacturers generally have instructions on the maintenance of the equipment together with parts list that if followed will assure proper operation and a longer life to the equipment.

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Chapter 14

Pesticide Formulation as Related to Environmental and Health Hazards

Freed, V.H. and Weilmuenster, E.

SUMMARY

Most chemicals used as pesticides must be formulated to achieve the properties needed for application and to reduce the concentration to the point where the chemical may be used. Two principal categories of formulation are liquid and dry. In each category, there are a number of different types, such as oil concentrates, water soluble concentrates, emulsifiable concentrates among the liquids, and thus, wettable powders and granulars among the dry. Use of the correct formulation can result in a more effective pest control with less chemical and greater human and environmental safety.


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INTRODUCTION

Over the past several decades pesticides have become extremely important tools in the improvement of agriculture and public health. The use of these chemicals for the control of insects, weeds, fungi and other pests has contributed greatly to increasing the supply of quality foods around the world. Equally important is the use of pesticides, particularly insecticides, for the control of insect vectors such as the tsetse fly and the mosquito in the protection of human health. Despite the very substantial efforts in recent years to find nonchemical means of pest control, pesticides remain one of the main methods of combating these pests. There is a consensus of opinion based on in-depth studies by a number of groups that chemicals will remain a principal weapon of pest control for the unforeseeable future.

Since pesticides are so important to the protection of our food supply and our health, they should be used in the safest and most effective manner. These chemicals are sophisticated tools of technology with biological effects not limited just to a particular pest, but may effect a wide variety of non-target organisms as well. Consequently, efforts to achieve safer and more efficient application and use of these chemicals are well worth our attention.

Background

Though pesticides are essential to health protection and agricultural production, they are not without their potential for harm if improperly used as pointed out in Chapter Two. We see four types of problems in the use of pesticides, namely: human poisoning, residues in foods and the environment, the development of resistant strains of pests, and in disposal of chemicals and containers. These problems arise not out of some unique property of the pesticides since they could occur with almost any chemical--natural or synthetic--if used in the same way. Rather, the problems arise out of misuse, over-reliance, inadequately designed formulations and application techniques, and improper disposal. A well accepted truism among pest control specialists is that something less than 10 percent of the chemical applied is required to control the pest with the balance of the chemical essentially lost to the environment.

Few chemicals may be used directly as the technical product for pest control (Green et al., 1977; UNIDO, 1972; Tahori, 1972). The technical chemical may be so insoluble that there is no means of applying it. Yet other chemicals are so highly toxic that until they are diluted in the appropriate formulation they cannot be applied in small enough amounts to control pests without undue hazard. Even with proper formulation and application, there is considerable waste entailed in the use of pesticides. Part is due to our inability to target the application directly on the pests. Another factor entailing use of more chemical than actually required to control pests, is the breakdown and loss of the chemical in the environment. Consequently, additional amounts of chemical must be used to achieve and maintain the concentration sufficient to control the pests over the desired period of time.

Pesticide Formulation Principles

Formulation is the process of transforming a chemical to be used as a pesticide into a product which can be applied by practical methods for effective, safe and economical use (UNIDO, 1972). A pesticide formulation is a mixture of one or more biologically active chemicals with inert ingredients. Because the great majority of all pesticidal chemicals require formulation to be used economically and effectively, the term "pesticide" throughout this chapter will refer to the finished product rather than to the active ingredient itself. Indeed, probably to the majority of users, the term pesticide is applied to the finished product. Pesticide formulation is the art and technology of developing a formulation of a pesticide.

Pesticide formulations are classified into two general types regarding physical form, e.g., the liquid and dry formulations (Green, 1977; Tahori, 1972). There are a number of varying types of formulations within each general classification. Also, many chemicals may be offered in more than one type of formulation other than just one. The formulation usually consists of a diluent such as a dust base or a solvent combined with other ingredients to provide the correct properties for application. Different formulations are called for depending upon the type and conditions of application, the target organism, and the nature of the pesticide itself. Among the factors which must be considered in formulating are: the method of application, the need for dilution of the active ingredient, safety in handling, reduction of loss through drift, vaporization or degradation, and adherence to the crop or soil being treated. A description of these types of formulations and their general purposes follows.

LIQUID FORMULATION TYPES

Oil Concentrates

Oil concentrates are liquid formulations containing, preferably, a high concentration of active ingredients. They may be used directly in ultra low volume application or after dilution to a practical concentration with an inexpensive hydrocarbon solvent as fuel oil or diesel oil. The concentration may be expressed either in terms of weight or active ingredient per unit volume of concentrate or in terms of percent by weight of active ingredient. It is necessary that the concentrate be miscible upon minimum agitation with the diluent to be used. Aromatic hydrocarbons such as xylene or heavy aromatic naphtha are generally used as solvents for the active ingredients in oil concentrates. There are pesticide chemicals whose solubility in these aromatics is so limited that aromatics are impractical as solvents. To overcome this limitation, it is necessary to use a more powerful solvent, e.g, isopropanol or cyclohexanone. The necessary qualification for the use of any of these

Liquid Concentrate

polar solvents is that the concentrate is miscible with the diluent oil which will be used.

Emulsifiable Concentrates

Emulsifiable concentrates are similar to the oil concentrates with the exception that they contain a surfactant or emulsifier to permit the dilution of the concentrate with water for practical application. For best results, the solvent system must be immiscible with water. The generally used solvents are xylene type, the heavy aromatic naphtha type or, occasionally when the solubility of the pesticidal chemical is sufficient, aliphatics of the kerosene range.

Because of their convenience for the user, emulsifiable concentrates may be considered the most popular form in which pesticide formulations are used. They are expected to perform well under a wide variety of conditions and to withstand a number of extremes of packaging and storage. Although the ideal emulsifiable concentrate is frequently sought, it is seldom attained. It will be shown that either compromises must be made or other useful alternative formulation types accepted as being more practical for certain pesticidal chemicals. Functionally, emulsifiable concentrates must disperse spontaneously in waters of all hardness and with the aid of gentle agitation remain uniformly dispersed throughout the spraying period.

Aqueous Concentrates

Aqueous concentrates are concentrates of pesticidal chemicals dissolved in water. The most frequently encountered pesticidal type found in this form is the salt of a herbicidal acid. Because the herbicidal acid is the nominal active ingredient, concentrations are generally expressed in terms of pounds of acid-equivalent per gallon. Since these active ingredients are soluble in water, there are generally no problems of miscibility, dispersability or suspendibility. The exception occurs when magnesium, calcium or iron of natural waters used for dilution may cause an insoluble precipitate; remedies do, however, exist for this situation.

Oil Solutions

Oil solutions are ready-to-use formulations containing, generally, a low-odor, colorless solvent of the kerosene type and a pesticide chemical in low concentration. The concentration of active ingredient is usually under 5 percent by weight. Oil solutions of insecticides are generally used for household or institutional insect control. In addition to low odor, these formulations must preferably be non-staining and have a high flash point to minimize the fire hazard.

Invert Emulsifiable Concentrates

Invert emulsifiable concentrates are distinguished from the normal emulsifiable concentrates by the fact that their dilution with water results in an emulsion in which the external or continuous phase of the emulsion is the oil portion, whereas the internal or discontinuous phase of the emulsion is water. These concentrates are used principally in the formulation of oil-soluble herbicidal esters. The solvent is usually an oil having relatively low vapor pressure. Field dilution is generally at a much lower ratio than that used for conventional emulsifiable concentrates and often less than ten parts of water to one part of concentrate by volume. The distinguishing feature of invert emulsions is that they form significantly larger droplets than conventional emulsifiable concentrates when emitted from special application equipment. Because the external phase contains an oil of relatively low vapor pressure, evaporation of the continuous phase is minimized (Fanger, 1974; Que Hee and Sutherland, 1974). As a result, there is no reduction in the size of the droplet from the time it emerges from the application equipment until it impinges on the target. The probability of drift of the particle during its fall through the air is, therefore, greatly reduced.

Flowable Concentrates

Flowable concentrates are another form of liquid formulation. They are really a hybrid, between the solid formulation and liquid formulation, in that the active ingredient is not dissolved in the liquid carrier, but rather very finely ground and dispersed as a solid suspension in the liquid carrier. In addition, there will often be a dispersing agent used in the formulation to keep the solid particulates from aggregating and precipitating from the liquid. The liquid carriers may be oil, usually an emulsifiable oil, so that the formulation may be further diluted with water. Where a particularly heavy oil has been used as the liquid phase, it often tends to reduce the loss by vaporization. In other instances, a solid material may be formed into a flowable concentrate in a water base, or in something like molasses. There is a formulation of carbaryl thus formulated. Flowables are handled a good deal like emulsifiable concentrates in that they pour and may be measured by volume for further dilution.

Mayonnaise (Thick Emulsion or Gel) Formulation

The "mayonnaise" or thick gel formulations are usually concentrated emulsions containing a high percentage of active ingredient. They are intended for subsequent dilution or emulsion in water for application. Such formulations are often not as convenient to measure in small quantity, and consequently are better adapted to large scale equipment.

DRY FORMULATIONS

The important dry formulation types are dust bases or dust concentrates, wettable powders, dusts, granules and pellets. All dry formulations with the exception of wettable powders are applied in the field in their dry form as dusts, granules, or pellets (UNIDO, 1972). The dust bases or concentrates and wettable powders are intended for further dilution to field strength before final application. In the case of dust bases, locally available low-cost diluents such as clay and talc are usually mixed with the concentrate at a regional formulation plant. Wettable powders are generally mixed with water before field application and then applied as a spray. In general, the packaging of dry formulations is considered to be less of a problem than

Dry Formulation, Wettable Powder

packaging of dry formulations. The characteristic differences of the dry formulations are shown in the following:

Dust Bases or Concentrates

Dust bases or dust concentrates are dry, free-flowing powders containing a high concentration of active ingredients which varies generally from 25 to 75 percent. Such products are seldom applied in this concentrated form. They are usually diluted or cut back to a practical concentration with a suitable inert material for final application in the field. Pesticide-fertilizer mixtures are often made by mixing the dust concentrate with the dry fertilizer. If granular fertilizers are being mixed with dust bases, a sticker is often necessary to prevent the segregation of the fine particles of the pesticide base which usually are below 200 mesh (74 μm) size.

Wettable Powders

Wettable powders are similar to dust bases except that they are formulated for dilution with water into a final spray. The quality of wettable powders is judged by the rapidity of wetting when mixed with water the suspendibility in water when mixed in practical dilutions for field application. The speed of wetting can be increased by the proper choice of wetting agents which reduce the interfacial tension between the particles and the water. Good suspendibility is attained by reducing the particle size, preferably to below 325 mesh (44 μm). Surfactants of the dispersant class are generally added to wettable powder as part of the regular formulation to prevent the agglomeration of particles and, in turn, decrease the rate of sedimentation, which is a function of particle size. Exceptionally fine particle size which further improves suspendibility is sometimes attained by air-milling the product to a particle size of 10 μm or less. Wettable powders are frequently used for the slurry treatment of seeds as well as in a variety of spraying techniques.

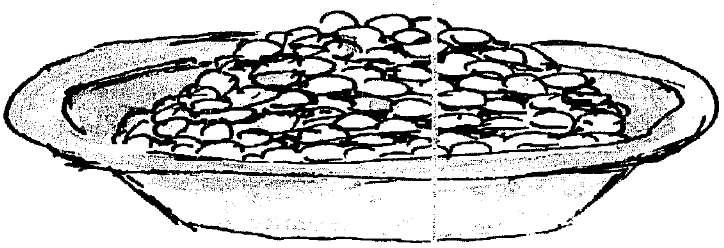
Dusts

Dusts are very finely powdered, dry pesticides. Dusts are formulated to field strength which may vary from one to ten percent active ingredient depending upon the potency of the pesticide and the rate of application. Dusts must be free-flowing so that they can be accurately metered in application equipment. Particle size may vary, although it is usually under 200 mesh (74 μm). For aerial application of dusts, the avoidance of drift is important; therefore, a moderate particle size and uniform distribution are necessary. Dust formulations applied by air or ground equipment are extremely advantageous when treating mature crops with dense foliage. This advantage is the inherent property of billowing around the foliage and covering the undersides of the leaves and the stems of the plant.

Granules

Granular pesticides are distinguished from powdered pesticides according to mesh size range. It is generally accepted that a granular pesticide is a product which is limited to a range from four mesh (United States standard sieve series) to 80 mesh. For any given material (for example, a product labeled 30/60), at least 90 percent of the finished product must be within this specified mesh range, and the remaining 10 percent may be distributed on either side of the specified mesh sizes. The presence of fines which may become airborne by a crosswind during application is generally considered to be objectionable in a granular product.

To be useful, granular pesticides must be non-caking during storage. To permit accurate application in metered application equipment, the granules must be free-flowing. Depending upon the field requirements, the granules may have fast or slow disintegration characteristics in the presence of moisture (Coppedge et al., 1975). The disintegration characteristics of granules after entering the soil have a direct bearing on the release rate of the pesticides.



Granular Formulation

The concentration of active ingredient in granular pesticides may vary from as little as one percent to as high as 42 percent as depending upon the properties of the active in ingredients, the characteristics of the carrier, or upon other factors such as the potency of the insecticide and the desired rate of application of the finished product.

Some granular formulations will be coated with a plastic, an oil, or a starch coating. This is often done where the active ingredient is highly toxic and it is desired to reduce the risk of exposure. In other cases, the coating is used to protect the active ingredient from loss or breakdown, or to provide a slower, sustained release.

Pellets

Pesticide pellets are dry pesticide formulations in which the particle size is larger than that specified for granular pesticide, e.g., greater than four mesh. There are no established maximum sizes for pellets, but in practice, diameters may be as large as 0.6 cm and possibly 1.3 cm. Pellets are generally formed by mixing the active ingredient with a suitable inert ingredient plus a binder, if necessary. The mixing is followed by pan-granulating to the desired size or extruding (and crushing, as required) to the desired size. Concentrations of active ingredients may range from a fraction of a percent as in the case of baits, in which as attractant, inert ingredient is used, to as high as 20 or 25 percent, if fertilizer is added.

OTHER TYPES OF FORMULATION

A number of other possible formulation types are used for special purposes. These are better classified by themselves rather than with the familiar types because of their unique physical form or their unusual application. Both liquid and dry formulation types are encountered.

Aerosols

Since their development for insect control during the early years of the Second World War, aerosol insecticides have become a familiar form of pesticide formulation. As generally understood, aerosols are solutions of an active ingredient in a suitable solvent plus a propellant which is a gas dissolved in the insecticide solution and/or contained under pressure in the aerosol dispenser. The type of spray pattern and particle size of the spray are controlled by the design of the nozzle which is used and by the pressure in the container which forces the concentrate through the nozzle. The internal pressure is determined by the properties of the propellant gas. There are many different approaches to the formulation and packaging of an aerosol pesticide product including both non-aqueous and aqueous solvent systems.

Seed Dressings

Seed dressing may be either a liquid or a dry type; indeed, there are variations within each type. Two of the most important requirements of a seed dressing are that the seed dressing must not interfere with the plantability of the seed; and that the seed dressing must not diminish the viability of the seed. In addition, it is most desirable (however, seldom attained) that the seed dressing is non-toxic and does not constitute an adulteration if the seed is later to be fed to livestock. Seed dressings must often contain a dye which colors the seed to indicate the chemical treatment. Certain seed dressings have been developed in dry concentrate form for the addition to seed grains in a planter box as controls of insects or diseases from the time of planting until after the seed has germinated. Wettable powder types of seed-treating formulations are used for the slurry treatment of feed as well as liquid types of certian emulsifiable concentrates and water-dispersible concentrates. The concentration of the active ingredient in seed-dressing formulations follows the same rules and limitations as other liquid and dry formulations.

Poison Baits

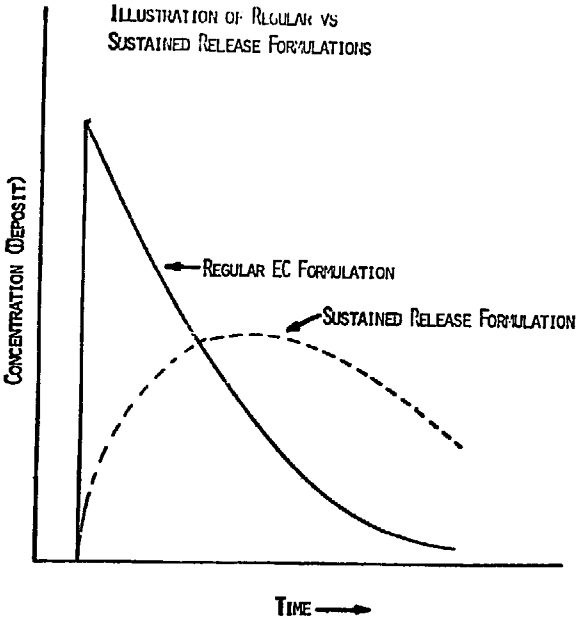
Poison baits are special formulations designed to attract and kill certain types of foraging insects and rodents. Poison baits are designed to preferentially lure and poison these pests near or in their natural environment. They are frequently used as a carrier to intercept the migration of insects such as locusts into grain fields. In orchards, rodenticide baits are placed around the tree trunks to prevent their attack by rats. Another form of bait is used in the so-called bait trap for the control of Japanese beetles in orchards or gardens and for the control of the Mediterranean fruit fly in citrus groves. Rodenticide baits in pellet or meal form are widely used for municipal and residential rat control and for the control of mice and rats in farm buildings and grain storage areas.

Poison baits have numerous physical forms and compositions. Where applicable, they have a distinct advantage in agricultural pest control by effectively reducing damage to agricultural crops by insects and rodents without the hazard of leaving a residue on the plant or crop to be protected.

Capsulated Formulations

The encapsulation of pesticides is a relatively new development with the principal objective of providing a controlled release rate for specific types of pesticide action. An encapsulated pesticide is essentially a very small mass of a pesticidal composition surrounded by a continuous shell or envelope of a coating material. Two factors to be considered in the selection of a coating material are the material's ability to dissolve or disintedisintegrate at a controlled rate by the action of certain environmental factors such as moisture or soil microorganisms. Particle diameter varies from a few µm to 0.3 cm or larger. Theoretically, the concentration of the active ingredient contained in the shell wall varies from a fraction of one percent up to and approaching a 100 percent active ingredient. Although the shell thickness may be very small in comparison to the diameter, the percentage of the encapsulating shell material increases as the particle size decreases. Similarly, the cost of an encapsulated pesticide ingredient varies inversely with the percent of concentration.

Microencapsulated



Fertilizer Mixtures

The use of fertilizer mixtures containing an insecticide and/or herbicide has become standard practice in agriculture as well as in gardening. Although the use of pesticides with dry fertilizer mixtures has become generally acceptable, the use of pesticides emulsified or dispersed in liquid fertilizers has not attained acceptance. The concentration of pesticide in dry fertilizer mixtures is generally quite low and usually under 0.5 percent. To meet field requirements in agricultural use, pesticide fertilizer mixtures are usually prepared by local fertilizer suppliers to order. Furthermore, because liquid fertilizers are usually applied by specialists, the special pesticide formulation must be added to a liquid fertilizer mixture prior to transportation to the field.

Pesticides are incorporated in dry fertilizers by spray impregnation or by blending of dust bases and granules. Because of the low concentration of pesticides in these products, great care must be exercised through efficient blending techniques to obtain a uniform product. Because of the trend towards the use of granular fertilizers, care must be taken in the formulation of these mixtures to prevent the possibility of segregation of the pesticide form the bulk of the fertilizer mixture. When using dust bases it is often necessary to use a sticker to prevent segregation of the powdered insesticide. Granular pesticides should be roughly of the same size or mass as the fertilizer granules to avoid separation. When adding oil concentrates of pesticides to granular fertilizers, only a small quantity of liquid concentrate should be used to avoid a wet or sticky product that can wet and migrate through the walls of the shipping bags. The quantity of liquid varies with the density and porosity of the granule.

Tank Mixes

Often, it will be desired to add other ingredients at the time of mixing ingredient, or it may be an additive to modify the performance of the main active ingredient. In some instances, additional surfactant or a sticker spreader may be added to enhance wetting and retention on the plant. In other instances, materials such as emulsified plastics, or emulsified oils (heavy petroleum or vegetable oils) may be added to reduce vaporization of both the carrier and the active ingredient and to improve persistence of the deposit.

It is possible in tank mixes to utilize a number of additives to reduce loss due to rain, e.g., emulsified plastics and heavy oils to slow down vapor losses and reduce photochemical decomposition. The agent or agents added at this time however, must be compatible with the original formulation and themselves emulsifiable or suspendable in the carrier. Usually such additives are used with emulsifiable concentrates but may be used with properly formulated wettable powders.

FACTORS TO BE CONSIDERED IN FORMULATION

In the past, the principal concern in developing a formulation was to put the active ingredient in such a form as to make possible the application. Having achieved this, the next goal in formulating was to ensure stability and shelf-life of the formula and only then was consideration given to modifying the formulation to maximize biological effectiveness. Only recently has more attention been given to developing formulation of greater ease of application and enhanced effectiveness. This has come about as we began to more fully appreciate the factors of both the formulation and the environment that could limit the effectiveness (NAS, 1975; UNIDO, 1972; Tahori, 1972).

As a background for proper formulation, it is desirable to review some of the environmental factors in pesticide behavior. The pesticide, to achieve the desired results, must be applied in the proper quantity at the right place and the correct time. There should be added one additional caveat to this; namely that the pesticide must then persist at the biologically effective concentration for a sufficient period of time to bring about pest control. The controlled release formulations are representative of just such an attempt to attain the required longevity of the pesticide deposit.

SOME FORMULATION ADDITIVES AND THEIR FUNCTION

Agent	Example	Function
Solvents	Petroleum Xylene Ketones	Dissolve and dilute active agents
Surfactants	Soaps Sulfonates Aryl polyoxy ethylene (Anionic, cationic, nonionic)	Emulsifiers Wetting agents
Thickeners	Methyl Cellulose Gums Water dispersible plastics	Increased viscosity and drop size Reduce drift

SOME FORMULATION ADDITIVES AND THEIR FUNCTION (continued)

Agent	Example	Function
Clays	Attaclay	Diluents and base for dusts
	Bentonite	Wettable powders and granulars
Stickers	Glyptal resins Plastics Terpene polymers	Enhance retention
Plastics	Micro-capsules	Carrier of pesticide reduce loss
	Dispersed (polybutyro acrylate)	Film former - reduce loss by wash-off Volatilization photodecomposition

A number of environmental factors influence the effectiveness of a pesticide application. Table 14-1 lists four of the more important factors. There are losses in the use of pesticides in part due to the foregoing factors and in part due to formulation and methods of application.

Table 14-1 - Environmental Factors Influencing Effectiveness of Pesticides

1. Temperature (height and variation)
2. Rainfall (moisture supply)
3. Light (intensity and quality)
4. Soil

Table 14-2 lists some of the sources of losses in the application and use of pesticides.

Table 14-2 - Factors Limiting Effectiveness of Pesticide Application

1. Loses during application
2. Degradation - Chemical
   Biological
   Photochemical
3. Vaporization
4. "Wash-off" with water
5. Adsorption
6. Leaching (in soil)

Consider the matter of drift of the pesticide during application. Any of the material not reaching the target area is ineffective and hence a waste. The drift, of course, is in part due to environmental factors, e.g., wind, the application technique, but perhaps to an unappreciated extent may be due to the formulation itself. Particles, particularly spray particles of less than 100 microns diameter, are very likely to drift off the target area even with a very mild wind condition (Byass and Lake, 1977; Dejonckheere, et al., 1976). To some extent, modifications of the volume of application, the carrier, the pressure and nozzle can control droplet size. However, a factor that may be of some importance is the vaporization of the carrier from the droplet resulting in a droplet of increasing diameter and hence, greater tendency to drift. The problem here then lies not with the chemical itself but with the carrier and the application. What is needed than if one were making an application of a spray under conditions of low relative humidity and high temperature, might be an agent in the formulation to ensure maintenance of larger droplet size. Some recent work has revealed a number of agents, notably the polyglycols and heavy oils, that may be effective at relatively low concentrations in doing just this.

To illustrate more fully the problem of evaporation of the carrier, consider the information in Table 14-3.

Table 14-3 - Evaporation Rate (H_2O, 86°F, 50% Relative Humidity)

Droplet Diameter in Microns	Lifetime (sec)	Distance of Fall
200	56 sec	69 ft
100	14 sec	6 ft
50	3.5 sec	1.25 in

One of the earliest problems to be dealt with by formulation was that of drift. With certain chemicals the drift from the target area posed a real problem. Engineers worked hard on the problem to develop application equipment to reduce drift, but until certain modifications of formulation were accomplished the equipment design alone was not enough to reduce the problem. One of the early attempts of formulation to reduce the drift problem was the use of the invert emulsion. The normal emulsion with which we are all familiar is oil in water - that is oil droplets dispersed in a continous water phase. However, by manipulation of the amount and kind of emulsifier and method of mixing we can produce the so-called invert emulsion or water in oil. This is a much thicker more vicous emuslion producing larger drop sizes. The larger the drop, of course, the less the drift. The next step in attempting to reduce drift, however, was the introduction of agents that would thicken normal sprays. A variety of these agents have been introduced and include such things as methyl cellulose, alginates, vegetable gums, and water dispersible plastics. More recently there has been developed a technique of application which rather than discrete spray particles utilizes a foam containing the chemical. Complex glycols and stabilizing agents are used to produce such materials in mechanical sprayers.

An encouraging development in pesticide formulation is that of microencapsulation (Collins, 1974). This idea came from the pharmaceutical industry where they were seeking to achieve sustained high concentration of a drug without having to administer frequent doses. Initially the drug was put in the form of a coated pill. The coating on the pill would then break down under either alkaline or acid conditions depending on where the physician wished the drug to be released. With the availability of some of the modern plastics, however, it was possible to encapsulate the drug in small beads where diffusion of the drug through the membrane of the capsule regulated the rate of release. By this means it has been possible with some drugs to achieve the same results with 1/10 dosage level. Adopting this method for formulation of agricultural chemicals, it was possible to reduce vapor losses, photodegradation, and at the same time increase the safety of those handling the material. Another example of where pesticides have been formulated in plastic are the plastic strips in which a pesticide is incorporated for sustained release.

Attention is now being given to additives and formulating ingredients to regulate the rate of release and extend the period of control. Other agents are being investigated for reducing vapor losses (Que Hee and Sutherland, 1974), prevent wash-off and slowing down biological degradation. It should soon be possible for example, to obtain granular formulations of system chemicals that will provide a sustained release that would extend the effective control period by two or three times.

Much remains to be done in formulating chemicals for specific uses and conditions. We now know enough about this problem to undertake such improvements, however. It is especially important to take full advantage of whatever modification of formulations possible to increase human safety, protect the environment, and conserve the limited supply of pesticides. It will be necessary to recognize, however, that pesticides designed for the temperate region are not necessarily the best for the tropics. The formulation must be designed for specific environmental conditions. With what we know today, this is not a formidable undertaking and is one that will yield handsome dividends.

SAFETY CONSIDERATIONS - HUMAN AND ENVIRONMENTAL

Handling and use of pesticides commonly results to a greater or lesser degree of exposure. The extent of exposure depends upon the care in handling and of the use of the appropriate protective clothing. The greatest risk of exposure is to those who work with the technical products and concentrates, such as in manufacturing, reformulating, or repackaging of concentrates without appropriate equipment. Studies of those who apply chemicals show that the likelihood of exposure in decreasing order is, mixer/loader, backsack sprayer, flagman, ground sprayer operator and aerial applicator.

The principal route of accidental exposure for those working with pesticides is dermal. Respiratory exposure to particulates and vapors under most conditions does not appear to be a serious source of intoxication. However, with highly volatile chemicals or in enclosed spaces, respiratory exposure becomes a more serious consideration. Oral ingestion of chemicals is most likely to be the result of carelessness or malignant intent.

While it may be difficult to completely avoid exposure, careful handling, the use of protective clothing, and proper choice of formulation for the particular use can help to minimize the risk of exposure. Thus, by utilizing the lowest possible concentration in the formulated product, compatible with the job to be done gives a margin of safety. Also, the formulation that is easily measured for the dilution to application strength is less likely to present an exposure than a formulation that may be difficult to weigh or measure. For example, it may be far easier to measure the volume of an emulsifiable concentrate than it would be to weight out the appropriate amount of dry formulation.

As noted earlier, dermal exposure is the most likely in handling, mixing, and applying pesticides. There is a good deal of difference between formulations as to the ease with which they penetrate the skin. Oil concentrates and emulsifiable concentrates of most chemicals penetrate far more readily than, let's say, a wettable powder, a dust, or granular formulation. The solid formulations, e.g., wettable powder, afford less skin penetration because of the adsorption of the chemical on the carrier, that is the clay or other material. Hence, granules and dust of relatively low concentration tend to be safer from a dermal exposure point of view than other formulations. Likewise, the coated granules are a means of formulating chemicals to minimize the likelihood of dermal exposure.

To some degree, environmental contamination can be avoided through choice of proper formulation. Thus, if drift is a problem during a spray applications, the addition of about 20 percent heavy petroleum oil or vegetable oil can insure a larger number of droplets, hence less drift. This would tend to avoid contamination of any non-target areas. In part also, the droplet size must be controlled by equipment setting and volume applied.

Dusts, because they are so finely ground, have a tendency to drift as well as do the fine spray particles. For controlled application, confine the maximum amount of material to the target area; spray application may be preferred over dusting. Where the dust is to be used, appropriate equipment and precautions should be taken to avoid drift problems.

In some instances, particularly with volatile materials, vaporization may be a problem. The environmental contamination in this case, is likely only to be to nearby areas, even where rather large amounts are applied. The rapid diffusion with any air movement results in dilusion and dissipation at any distance from the treated area. However, though the localized contamination may be a problem, special formulations and applications can be used to minimize the problem. For example, a somewhat volatile product might be applied as a low concentration granular, or applied with an additive that reduced the rate of vapor loss.

Attention to appropriate formulation, then, can result not only in safer more effective pest control, but also avoid human exposure and environmental contamination. Formulation may either be a commercial product, or the result of a tank mix with appropriate additives to achieve the desired properties.

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Chapter 15

Transport, Storage and Disposal

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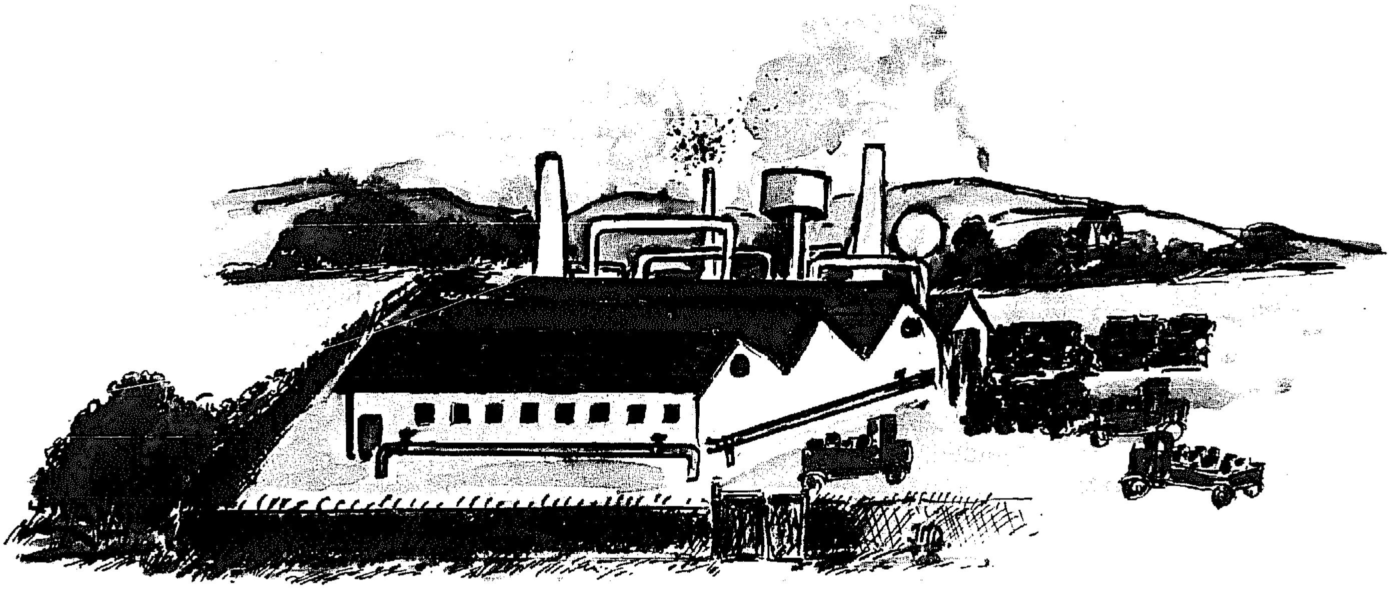


SUMMARY

Proper disposal of excess, or waste pesticides and pesticide containers is very important. Improper disposal can result in a hazard to humans and contamination of the environment. There are a number of practices that can be followed to provide safer disposal. For large facilities such as a manufacturer, incineration, wet oxidation or trickling filter degradation can be used. For smaller operations, adsorbent filters, chemical treatment, oxidation ponds and other treatments offer a possibility. For other than large industrial operations, such practices as adsorption on charcoal or resin and careful land disposal affords a practical means of disposal if properly practiced.

INTRODUCTION

The problem of pollution is always present in the manufacture, formulation use and disposal of pesticides (Lawless, et al., 1972). These products, to be sure, are of vital importance to agriculture and for control of many disease carrying vectors, but can cause serious problems as contaminants. Despite the problems that we may encounter and have to solve in the use of pesticides, there is no question but what we will have to continue to use them to assure food production and health protection.

Many of the problems experienced with pesticide contamination come about through poor systems of handling, use and regulation. As a result we find that pesticides may cause problems of too high residues on crops, pollution of water and soil, the development of resistance in target organisms, poisoning of humans and problems of disposal.

Many of the problems with pesticides could be avoided through the application of some simple common sense practices. The large manufacturing operation usually has or should have the technical knowledge, equipment, and the desire to control its pollution problems (Pollution Control Technology, 1974). It is with the small formulator, distributor and user of pesticides that pollution problems very often occur. Solution to these problems begins with education or training, wise selection of chemicals and formulations, intelligent use and disposal, and effective regulation. A few comments on each of these practices is well in order.

REGULATION

Just as governments have laws and regulations for other businesses, so laws and regulations are needed for the importation, manufacture, formulation, distribution, use and disposal of pesticides. Well designed and effectively enforced regulations can be helpful in reducing problems of contamination or pollution. The regulations need not be extensive or complex, but should be designed to accomplish specific purposes. Further, they should be helpful to both the user and the chemical industry and implemented in such way as to achieve that end.

Regulations should have the purpose of ensuring the importation or manufacture of the required products that are effective for the intended uses. They should then be administered to guarantee that the product on the market contains the amount of active ingredient of the proper quality that is specified. Next there should be concern for how the chemical is packaged and sold, and how the chemical is labeled. By all means, regulations should give guidance in developing the proper size and type of package for the ingredient, the climate, and the market, and discourage the packaging in odd containers. The requirements for labeling should include that it is in the language and symbols that would be understood by the user. The label should include not only directions for dilution and use, but also emergency medical treatment should poisoning occur.

It is in the distribution of pesticides that often problems of contamination begin to arise. These may come about when a dealer repackages the chemical, sells a chemical to person that is not trained or equipped to apply it, or otherwise has poor distribution practices. Another problem in distribution is the matter of storage and shipment. Having the proper storage area is also important with pesticides. Pesticides, after all, are poisons and should be handled as such. This means the storage area should be away from other operations and in a location that, should an accident or spill occur, it will not result in contamination of streams, groundwater, or areas that humans may frequent. Appropriate regulations are needed to ensure against all of these problems.

Finally, because there will always be excess containers and waste pesticides, regulations are needed for disposal. Guidelines are required in the form of regulations for both methods of disposal and sites that are suitable for disposal. Many of these containers and wastes have to be disposed of in the soil, in which case the site should be selected where there is not likely to be contamination of water nor accessible to humans or animals, and where the chemicals will degrade to safe products.

HAZARDS IN THE MOVEMENT AND STORAGE OF PESTICIDES

Most pesticide products present hazards during handling, transportation and storage on account of their toxicity to humans, animals and the environment. Some pesticides are highly flammable and/or may be converted to toxic gases upon burning.

For these reasons, the transportation and storage of pesticides is subject to laws and regulations by many countries, states or other government units. In the acquisition and movement of pesticides, it is important for the persons or agencies responsible to be fully cognizant of all applicable laws and regulations, and to assure full compliance.

Major hazards associated with pesticides handling, transportation and storage, and precautions to minimize these are discussed in the following sections.

LEAKS AND SPILLS IN TRANSIT

The movement and storage of pesticides is associated with the risk of leaks or spills from defective containers, seams or closures, or from puncturing, breakage or tearing of containers. Pesticides must not be shipped in the same containers or compartments with cargo that could become a hazard if contaminated, such as food, clothing, drugs, toys, cosmetics, or household furnishings (Lawless, et al., 1972). There have been a number of poisoning cases where particularly food and clothing have become contaminated in shipment because the chemical and the other item(s) were in the same hold or truck.

Pesticide spills may be acutely dangerous to transportation and warehousing personnel, people involved in cleanup operations, and people or animals in the vicinity of the spill. Serious secondary dangers arise if other cargo becomes contaminated. In addition, water suplies and other elements of the environment may become contaminated by the spilled toxic material directly, and/or by cleanup operations. The importance of preventing spills and of taking all necessary steps and preparations for the proper handling and protection of shipments of toxic pesticides cannot be overemphasized. Such steps and preparations should include the following:

1. Prior to or during loading, each pesticide container should be inspected for tightness of closure or seal, and for any evidence of leakage around the closure, on the top, along the sides, on the bottom, and under the container. Containers showing any evidence of leakage should not be loaded. If a high percentage of containers in a shipment show evidence of leakage, the entire shipment should not be loaded.

2. Pesticide containers should be loaded into the carrier and secured inside the cargo compartment in such a way that they are held in place securely, without possibility of damaging each other, or damaging or being damaged in transit by other cargo. Toxic pesticides must not be shipped in the same compartment with cargo that could become a hazard if contaminated by the pesticide(s).

3. In the loading and unloading of pesticides, only equipment and tools which will not damage the pesticide containers should be used. In particular, the use of hooks which may puncture or tear pesticide containers must not be employed.

All personnel involved in the loading, transporting and unloading of pesticides should be fully informed about the toxicity and the hazard potential of the pesticide(s) they are handling. They should be provided with information on how to deal with spills of the particular chemical(s) they are handling, and whom to call in an emergency for (a) medical and (b) technical information.

Personnel, especially supervisory persons, should be trained in appropriate first aid and rescue procedures. All necessary safety, first aid and rescue equipment and supplies which may be required should be available and readily accessible before the handling of pesticide shipments begin. Depending on the toxicity of the material being handled, such necessary supplies may include all-purpose gas masks; respirators; goggles or face shield for eye and face protection; waterproof and impervious complete outer clothing, including gloves, boots, hat and long-sleeved, buttoned coat or suit completely covering the worker; adequate emergency water supply for washing off corrosive or toxic materials getting on the skin; and facilities for washing eyes such as fixed or portable eyewash fountains.

The facility where pesticides are being handled should have access to a qualified physician who has been informed beforehand about the nature and toxicity of the pesticides involved.

Careful observation of these precautions is especially important in the transfer of large quantities of pesticides from docks to ships or vice versa. Crane operators, stevedores and other workers must be instructed to handle the material with extreme care. Dockside spillage or contamination of the cargo must be prevented. Emergency cleanup supplies and equipment should be available before movement of the pesticide shipment starts. (See section on spills in storage for more detail.)

Port and Public Health Officials should be notified of arriving pesticide shipments. They should inspect the conditions of the shipment in the shiphold prior to unloading and supervise the unloading operation, especially the proper cleanup and decontamination of any spillage.

FLAMMABILITY AND FIRES

Liquid pesticide products, especially those containing organic solvents with low temperature flash points, present special hazards because of their flammability. Some dry powder formulations may also present fire or explosion hazards.

In the United States, pesticides with low flash points are required to carry the following warning statements:

- -- Flash point at or below 20°F (-6.7°C): "Danger - extremely flammable! Keep away from fire, sparks, and heated surfaces."
- -- Flash points between 20°F and 80°F (-6.7° to 26.7°C): "Warning - flammable! Keep away from heat and open flame."
- -- Flash point between 80°F and 150°F (26.7° to 65.5°C): "Do not use or store near heat or open flame."

Persons handling pesticide shipments should check labels for these warnings and make certain that products are handled and stored in accordance with these directions which are intended to prevent fires and explosions.

Pesticides are especially dangerous when they become involved in fires. Highly flammable products will readily ignite and burn, or explode when overheated. Finely divided dusts or powders such as sulfur will ignite almost as easily as gases or vapors and thus present an explosive hazard. Aerosol containers will explode when overheated.

Fumes or smoke given off by burning pesticides may be highly toxic to firefighters and persons in the vicinity of the fire. They may also be highly poisonous to plants or animals.

Runoff water from fighting pesticide fires is likely to be highly toxic. Such water may carry heavy concentrations of pesticides and be toxic to humans, animals, plants and the environment at large. Contamination of streams, rivers, ponds, lakes or other bodies of water may cause grave secondary hazards and magnify the toxicity hazards.

It is obvious that every possible precaution must be taken to prevent pesticide fires. This is an important consideration in the construction, selection and use of storage areas for pesticides.

In case of an actual fire involving pesticides, the firemen fighting the fire and police on duty in the area must be given full information on the kinds, quantities and location of pesticide stocks in or near the area affected by the fire. Firemen must wear protective clothing over the entire body including rubber boots, gloves, hat and coat, and self-contained breathing equipment for protection against toxic fumes or smoke. The fire should be attacked from upwind or at right angles. Use of water should be kept to the absolute minimum so as to avoid toxic runoff. If possible, the affected area should be diked to prevent water runoff.

Residents and other persons in the area, especially downwind from the fire, may have to be evacuated. All unauthorized persons must be kept out of the fire area and the vicinity.

A qualified physician familiar with pesticide problems should be notified immediately and stand by to assist firefighters and others who may be poisoned. All persons who become exposed to toxic pesticides or toxic fumes or smoke should take immediate action to remove the toxicant(s) by thorough washing with large volumes of soap and water and should be checked for symptoms of poisoning.

The affected area should be roped off and posted to prevent entry by all unauthorized persons. This protection must be kept in effect until after cleanup.

Cleanup operations after the fire should be directed and carried out by qualified personnel well informed about the toxicity, the chemical, physical and other pertinent properties of the pesticide(s) involved in the fire. If this information is not available, it should first be obtained from the manufacturers, their representatives, or appropriate national or local government agencies.

Cleanup operations must be closely coordinated with local police, public health, environmental protection and other appropriate agencies.

Items which are sometimes overlooked during or after a fire or other catastrophic event involving pesticides include the following:

-- Footwear may become contaminated and absorb pesticides both on the inside and outside. Leather and lighter footwear should be discarded if contamination has taken place because it cannot be effectively decontaminated. Heavy rubber boots such as those worn by firemen must be thoroughly washed and cleaned inside and out before re-use.

-- All personal clothing, protective clothing, respirators, etc., must be carefully washed or cleaned before re-use. If such items are heavily contaminated, they should be properly disposed of because otherwise, their cleaning may create new hazards of toxicity or contamination.

-- Special care must be taken not to track pesticides or toxic residues out of the area.

-- Mechanized equipment should be used for cleanup as much as possible to minimize human contact with contaminated material.

-- Toxic debris must be treated and disposed of in the same manner as toxic pesticides and pesticide containers. (See that section of this manual for further details.)

-- All operations, including decontamination of tools, vehicles, equipment, etc., should be conducted in a such a way as to avoid toxicity or environmental contamination hazards from the cleanup operations.

FLOODS

Stored pesticides are liable to create grave problems if they become involved in floods. Products packaged in watertight containers may be swept or float away and may break and spill their contents upon hitting an obstacle, or later on upon deterioration of the container. Products packaged in paper, cardboard, or similar material may release the contained pesticide very quickly after getting soaked. In either event, and depending upon the toxicity of the pesticide(s) involved, grave danger from water contamination may result.

Pesticide stocks which have become soaked may become unusable and may present extremely difficult problems of handling and disposal even after they dry out again.

Every precaution must be taken to protect stored pesticides from flood waters. Pesticides must not be stored or kept in areas, buildings or parts of buildings (basements) which may be subject to flooding.

If pesticide inventories nevertheless become involved in floods, a problem exists which requires very careful evaluation and handling by the joint efforts of public health, environmental protection and police officials. If any pesticide quantities have been carried away from the storage site, every effort must be made to locate and secure them and to prevent further spillage. If water has become contaminated, persons or communities downstream must be warned, especially communities, farms, livestock operations, irrigation districts or other organizations drawing their water supplies from the contaminated body of water.

The manufacturer(s) of the pesticide(s) concerned should be contacted for information on the most effective decontamination methods and for any other assistance they may be able to render in coping with the emergency.

STORAGE ON THE FARM

Storage Using Eaves of Shed

Spills and leaky containers can contribute to contamination of food and water and result in unnecessary exposure to human beings. For that reason, pesticides should be stored in a safe place, preferably in a separate building or in a cupboard that can be closed and locked if possible. The storage area should be well away from water supplies and streams so that in the event of an accident, these are not contaminated. Even for the small farmer, it is desirable to see that there is proper equipment available should there be a spill. This would include an absorbent material or even pails of dry soil that could be immediately thrown on the spilled area to absorb the chemical. Other items should include rubber gloves to be used in handling the chemical, particularly when mixing and, if necessary, the appropriate masks and other protective clothing. While it is more difficult and time consuming to carry the water to where the chemicals will be mixed, it is better that, than to have a stream or well contaminated by the chemical.

SPILLS IN STORAGE

In each storage facility, precautions should be taken against spills of chemicals. This is particularly true of the highly toxic organophosphates. However, the spill of any chemical no matter how innocuous it appears to be should be treated as a hazard. It is highly recommended that in each storage facility or anywhere that quantities of chemicals are handled, there be an ample and readily accessible supply of charcoal and various clays to adsorb the chemical. In addition, there should be a supply of lime or calcium carbonate to neutralize those materials such as the phosphates and carbamates that are readily broken down by lime. If large quantities of liquid are involved, it is desirable to have an adsorbent material such as vermiculite or a clay available to assist the carbon in the adsorption. Appropriate protective clothing such as masks, gloves, rubber boots, and clothing should be available for the workers that must deal with such spills (Kennedy, et al., 1969; Powers, 1976; Pollution Control Technology, 1974).

Supplies for Spill Cleanup

The material used to adsorb the spilled material should be disposed of in the same manner as excess pesticides. Further, where the area must be flushed to complete the cleanup, the water should be drained into a decontamination basin or sump and not into sewers or streams. The chemical may be further degraded in the sump by addition of other chemicals, e.g. lime and adsorbents.

If the plant is properly constructed, the spills and leaks will be contained on the concrete floor where they may be absorbed with carbon or a clay, neutralized with lime and this waste then disposed of by soil degradation at an appropriate site. If such spills are to be flushed into a drain, the drain should be fitted with a charcoal filter and the effluent water led into a pond or an additional treatment facility before it is released into the sewer system or discharged into a stream. Such facilities as the filter and treatment are not at all expensive and can usually be fabricated right at the plant.

Carbon Filter for Pollution Prevention

A special warning should be issued about storage and formulating facilities in reference to the type of floor on which these operations are carried out. Several times in this presentation we mentioned that concrete floors should be used. This is to avoid having a floor into which the chemical can soak and later be released as vapor or picked up on water in the case of a flood. Wooden floors or earthen floors adsorb and hold the chemical and because of the extremely high concentrations, little or no breakdown occurs. Consequently, the risk of human exposure in this situation is high.

CROSS CONTAMINATION

Some pesticides are volatile and may contaminate other pesticides. Herbicides or other highly volatile pesticides must not be transported or stored with other pesticides.

Fumes from volatile pesticides may not only be harmful as contaminants of other products, but may also cause direct injury to persons or animals in the vicinity or to plants, seeds, etc. Special care is advised in situations where volatile herbicides are handled or stored in the vicinity of greenhouses or other areas containing sensitive plants.

ODOR

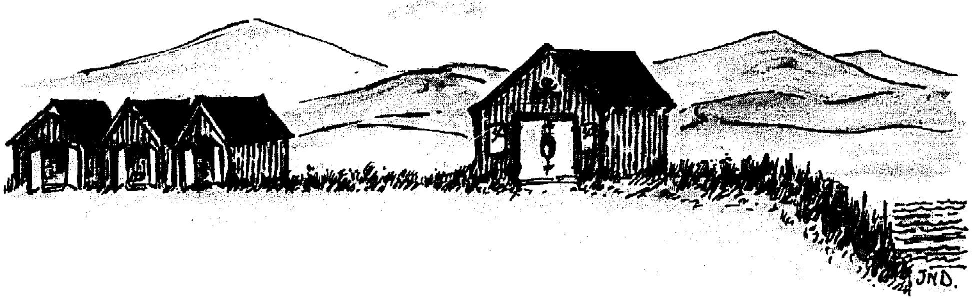
Some pesticides emit odors. Where such odors are present in the vicinity of pesticide stocks, they may indicate a leak or spill, or the presence of improperly tightened or defective closures. They may also indicate decomposition or other deterioration of the product. Some pesticides become increasingly malodorous upon deterioration.

Pesticide stocks with an odor problem should first be examined for a possible spillage, leakage or deterioration problem. If examination shows that no other corrective action is required, an odor problem may be alleviated by holding temperatures in the storage area down and/or by installation of exhaust fans. Such fans must be located carefully and their exhausts may have to be channeled through scrubbers or charcoal filters, made by filling a section of air duct pipe with granular charcoal, in order to avoid environmental contamination.

PESTICIDE STORAGE

All pesticides, regardless of quantity, should always be stored in the original, labeled container with the label plainly visible. Pesticides must never be stored in any other containers, especially not in old bottles, food or other containers where they could be mistaken for food, beverage, drugs, etc., for humans or animals. Pesticides must not be stored near food, feed, or other items which may become contaminated by spilled material, volatile pesticides, odors, etc.

Larger quantities of pesticides should be stored in warehouses or warehouse areas specifically designated for this purpose. Pesticide storage areas should have concrete floors with drainage to a sump or other holding area where contaminated water can be decontaminated before release. Earthen or wooden floors are not suitable because they cannot be adequately decontaminated. The storage area should be dry and well ventilated. The storage building should be located on high enough ground as to be above any floor. Some pesticides must not be stored at temperatures below freezing, while others cannot be stored at higher temperatures. Specific storage requirements must be complied with for each pesticide product. These requirements should be ascertained from the label.



Locked Storage Facility

Pesticide storage areas should be locked, or other suitable steps be taken to prevent theft, and to prevent unauthorized persons, especially children, from entering. Pesticide storage areas should be marked with prominent, waterproof signs over each entrance indicating the material stored.

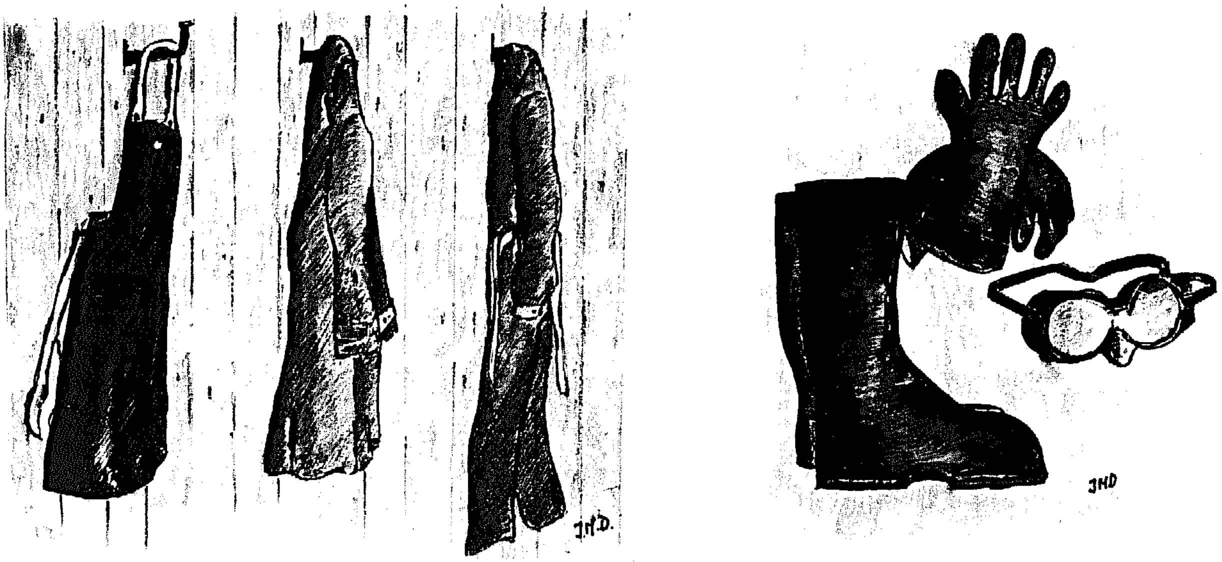
A complete inventory of all pesticides in the storage area is essential. The age of pesticides in inventory should be monitored to prevent them from becoming unusable due to deterioration. In case of emergencies, a list of the products stored and their locations should be given to safety and fire department personnel.

All pesticide stocks must be examined periodically for leaks, spills, or any signs of deterioration. Any spilled material, broken containers, etc., should be completely removed, and the area decontaminated and cleaned promptly.

Steps should be taken to make certain that runoff water from cleaning and housekeeping activities will not contaminate residential areas, livestock feeding areas, or bodies of water. Pesticide storage areas should be diked or otherwise arranged in such a way that all runoff water can be trapped in a suitable pool or sump for proper decontamination and disposal.

Since pesticide fires present grave dangers, as discussed previously, fire prevention and protection measures in pesticide storage and warehousing areas are particularly important. These should include effective fire detection systems and use of spark-proof electrical wiring and equipment such as safety lamps, motors, switches, outlets, etc. Pesticides should be kept away from steam lines, heating units, exposed windows and other heat sources.

Appropriate fire fighting and safety equipment of adequate capacity and in adequate numbers should be available throughout the pesticide storage area, and all operating personnel should be thoroughly familiarized with its use not only in theory, but also by regular practice drills. Protective and safety equipment such as fire blankets, complete protective clothing including hats, boots, coats or suits; gas masks, respirators, face shields, etc., should be readily accessible, regularly checked and maintained in workable condition.



Clothes for Spill Cleanup

Local police, fire department, public health, environmental protection and other concerned agencies should be familiarized with the pesticide storage area, with the facility's operating procedures, and with the safety program and equipment.

The safety program should include anticipation of, and planning for, all emergencies which may arise, including but not limited to fires, floods, tornadoes, hurricanes, typhoons, theft, abnormally hot or cold weather, and other calamities. The probable direct and indirect effects of each potential calamity should be anticipated as completely as possible. Steps should be taken to prevent calamitous results to the largest extent possible, and contingency plans be made on how to deal with catastrophies involving the stored pesticides if and when they occur.

All workers and supervisory personnel involved in the handling, transportation and storage of pesticides should have ready access to qualified medical aid, to information on the chemical, physical and toxicological properties of the pesticide products, including detailed information on how to deal with spills.

STABILITY OF PESTICIDES

Many pesticides, no matter how well manufactured, formulated and packaged, deteriorate upon storage, especially under conditions of high temperature and high humidity. Such deterioration may include loss of active ingredient due to chemical decomposition; loss of emulsifiability in the case of emulsifiable concentrates; compaction and caking in the case of dry formulations, and corrosion or other loss of integrity of containers and labeling. Some pesticides convert into more toxic substances upon aging.

In general, formulations containing low concentrations of active ingredilents tend to lose active ingredients more rapidly than more concentrated pesticide forms. Some liquid pesticide products tend to develop gas upon deterioration which may make containers very hazardous to open and lead to eventual explosive rupture of containers.

It is important in the purchasing of pesticides for use in other countries and arranging for their transportation and delivery, to be aware of these problems. Acquisition of pesticides for use in tropical countries should be scheduled and implemented so as to minimize storage time, and to move the pesticide from the original supplier to its ultimate use as expeditiously as possible. Sometimes, pesticides will have to be held over from one season to the next. Such storage should be held to a minimum, and under no circumstances should the time lapse between manufacturer and use exceed 24 months.

DISPOSAL OF CHEMICALS AND USED PESTICIDE CONTAINERS

Often in formulation and use of pesticides, there will be by-products of the parent chemical that must be disposed of. This may be an excess of spray mixture over and above that which is needed, distressed stock, that is, chemical that can no longer be used, or chemical that has deteriorated over a period of time. Similarly, during the use of chemicals, containers will be emptied and these pose a problem of disposal. Disposing of chemicals or containers in the safest possible manner is no simple problem. The method used must be adapted to the facilities available and the conditions so as not to create problems of human exposure or environmental pollution (Kennedy, et al., 1969; Lamberton, et al., 1976; Lawless, et al., 1975).

In the disposal of chemicals or containers, it is necessary to observe due precautions to avoid human exposure since most of these chemicals will be in a concentrated form. Moreover, disposal may involve sizable quantities of chemicals - from a few grams to a few hundred kilograms in the case of a formulating plant or a large agricultural operation. With such quantities, there is not only the problem of human exposure, but also that of environmental pollution to be avoided.

In selecting the manner and place of disposal, a number of factors must be considered. First of all, it must be recognized that any chemical in sufficient concentration may be toxic. This is a basic fact and applies whether dealing with an individual organism, such as a human, a population of organisms, such as fish in a river, or dealing with the environment. If we are dealing with a toxic chemical, this point is obvious. It becomes somewhat less obvious where the chemical has been categorized as one of lower toxicity. Thus, in the disposal, it is essential to avoid building up high enough concentrations to cause untoward effects.

In disposal of chemicals a number of questions should be asked. The first question to be asked is, "What are the physical properties of the compound? Is it highly volatile? Is it water soluble? Does it break down readily with heat or is it attacked by microorganisms?" Then there is the question of toxicity. "Is it acutely toxic, or does it accumulate in organisms and bring about chronic effects?"

Next there are the questions of the place of disposal in relation to humans and the ecosystem. "Is the site proposed near human habitation? Is it near water, either bodies of water such as lakes and streams or a groundwater aquifer? What is the prevailing wind direction?" Also to be considered are climatic factors such as temperature and rainfall.

Finally, to be weighed into the equation for disposal is the amount of chemical involved. Very small lots of chemical may be safely disposed of in one manner but much larger lots of the same chemical could pose serious problems if disposed of in the same manner.

For the most part, what is presented here is intended to provide suggestions for disposal of relatively small lots of chemical and containers. The information would be applicable to the agricultural operation or small formulating plants. The problems of disposal of larger quantities of chemicals such as would be encountered by the manufacturing plants, are different both in magnitude and character. This should be dealt with by teams of experts.

METHODS OF DISPOSAL OF CHEMICAL

There are a number of methods of disposing of comparatively small lots of chemicals. Depending upon the nature of the chemical, its biological properties, and other factors, each method will have its own advantages and disadvantages. The attempt below is to give a brief description of the different methods that have been considered at one time or another.

Use as Intended:

Use chemicals as they are intended to be used. Purchase only what is necessary.

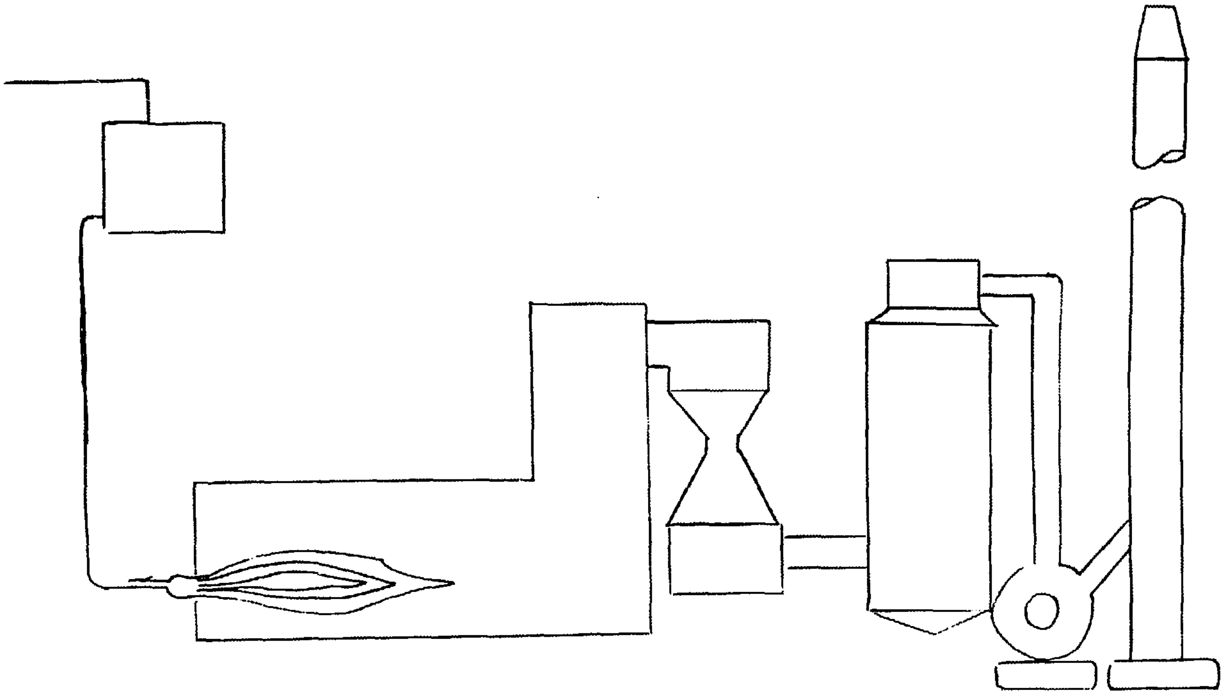
Perhaps the most effective and economic means of disposing of a chemical is to use it as it is intended to be used. The low concentration per unit area is such that the degradation forces such as photochemical reactions, biological degradation, etc., will bring about the ultimate disposal. This means, however, that the chemicals should be used in the safest and most prudent manner so as to avoid problems. If this is the method of disposal to be used, no more chemical than is needed should be purchased. By avoiding excess supplies that must be stored from year to year, there need be no concern with deterioration of the chemical, hazard in storage, and consequent need to dispose of the chemical.

Recovery and Recycling:

This method of disposing distressed stock or excessive supply is available only to the larger formulator or manufacturer. However, there are such instances where useful and valuable chemicals can be recovered for reuse by employing the proper chemical manipulations. It is not a method advised for poorly equipped facilities because of the need to use appropriate solvents, adsorbents, and carrying out complex chemical manipulation. Recovery is probably not suitable unless there is a sufficiently large quantity of the material on hand. Thus, it is likely not to be economical for the formulator or manufacturer to attempt to retrieve small lots of chemicals from widely scattered spots for reprocessing.

Incinerator:

Burning, or incineration, is of course an ultimate way of disposing of chemical (Kennedy, et al., 1969; Pollution Control Technology, 1974). With effective incineration, the organic chemicals are converted to carbon dioxide, water, sulfur oxides, hydrochloric acid, and other simple inorganic compounds. However, incineration is not an easy nor cheap method of disposal. It requires large complex and very expensive equipment to be done properly. For example, an incinerator that provides proper combustion of pesticides must have a flame temperature of 900°-1200°C and a fire box in which the chemical will have a residence time of at least two to ten seconds depending on the nature of the chemical. In addition, the appropriate pollution control devices needed on such incinerators to trap the acids and other materials formed into combustion to avoid both damage to the incinerator and environmental pollution (Powers, 1976; Pollution Control Technology, 1974). Costs for this type of installation to incinerate organic chemicals can run between one and several million dollars.



Commercial Waste Incinerator

Open burning such as in open pit garbage disposal or an open fire in a field is not recommended as a means of disposing of chemicals. The temperature attained in such fires is too low to complete the destruction of the chemical and may actually result in the formation of even more toxic products. Moreover, the nature of open fires result in vaporization of some of the chemicals with consequent pollution of the air. In experiments with such open burning, it was found that the concentration of parathion in the air was several times higher than the allowed standard, and in fact, concentrations near the fire reached dangerously toxic levels. For this reason, open burning is not recommended for disposal of either chemicals or containers such as paper and plastic bags.

Table 15-1. Temperatures Required to Decompose 98% or More of a Pesticide*

Compound	Temperature °C
DDT	600
Picloram	900
Malathion	>1000
Diuron	>1000
Paraquat	700
2,4-D	600

*Residue Reviews, 29:89, 1969.

Deep Well Injection:

Several years ago a practice of chemical disposal by deep well injection was considered as a means of disposal for certain chemicals. The practice was not widely adopted because of the few geologic formations suitable for this type of disposal. In addition, the cost of drilling and operating such wells is quite large. It turned out that this was a fortunate circumstance since the deep well injection has proved to present problems of water contamination as was discovered where the method was used for 2,4-D. Because of the cost and the environmental hazard to water supplies, deep well injection as a disposal method is no longer considered very limited (Lawless, et al., 1975; Powers, 1976).

Disposal in Water:

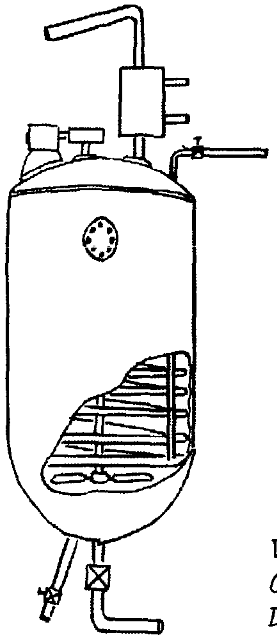
For many years, there was a saying that the "solution to pollution is dilution," and as a consequence, sewers, streams, lakes and even the ocean were widely used for disposal. While this method of disposal is cheap, it in effect, merely transfers the problem from one place to another. If the disposal is through an urban sewer system that utilizes primary and secondary treatment, the chemical may cause problems in the sewage treatment plant. If little or no treatment is employed, it is probable that the chemical will be dumped along with the sewage water into rivers or other bodies of water. If, on the other hand, it is disposed of on land, it may result in soil contamination and if volatile, air contamination.

Direct dumping of chemicals into a body or stream of water merely transfers the pollution problem downstream. This can result in contamination of someone's drinking water, residues in the aquatic biota, and even destruction of the organisms. Indeed, there are cases today where large lakes and even seas, such as the Baltic and Mediterranean have become seriously polluted in certain areas due to contamination of chemical in these bodies of water.

A few years ago, it was thought that the oceans could be used as a site for disposal of both solid wastes and chemicals. Subsequent studies have shown this to be a poor practice.

In general, it can be said that there should be no disposal of chemicals in sewers or in bodies of water without prior treatment because of the pollution problems it poses. Where dealing with the water effluent from a manufacturing or formulating plant, the water effluent should be carefully treated to remove the chemical.

Chemical Treatment:



Vessel for Chemical Destruction

Many of the pesticides in use today can be broken down quite readily by appropriate chemical treatment. In some instances, this is a rather simple reaction, in other cases, elaborate processes are required. It is important to remember that proper precautions be observed in attempting chemical degradation of pesticides. In the first instance, there is the matter of careful handling of the material and providing protective clothing and devices to prevent exposure. Secondly, many of the reactions are spontaneous and may generate considerable heat or even explosive forces unless properly controlled (Lawless et al., 1975; Powers, 1976).

One of the chemical treatments that has been proposed for chemical disposal is treatment with chlorine gas. This reaction will degrade a compound such as DDT to chloroform and carbon tetrachloride as seen in the following reaction.

Chlorinolysis

$$C_8H_9Cl_2 + 18Cl_2 \rightarrow 8CCl_4 + 9HCl$$

While this reaction does indeed destroy the parent compound, it generates a new highly chlorinated product that must be disposed of, namely carbon tetrachloride. For this reason, chlorinolysis is not widely used except in dealing with a highly toxic product in a chemical plant where the carbon tetrachloride can either be used or safely disposed of by other means.

Hydrolysis or reaction with water is the characteristic of the organophosphate and carbamate insecticides and a number of herbicides. In hydrolysis, the parent compound is usually converted to a product having much lower biological activity. The reaction products can then be disposed of in soil or by other means.

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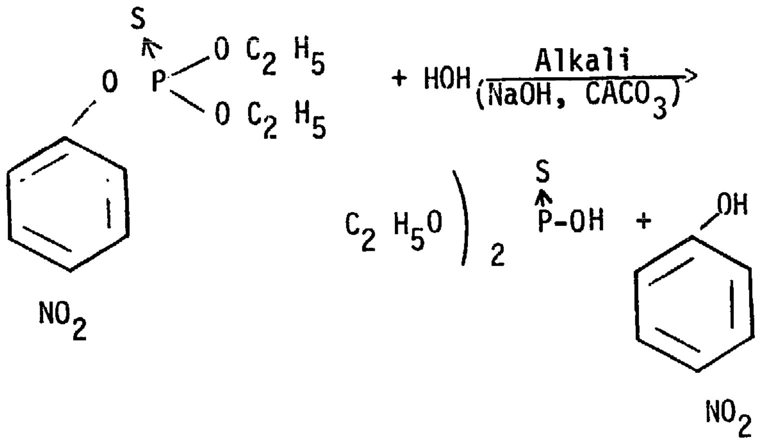
While we speak of hydrolysis of compounds such as the organophosphates, carbamates, esters, and amides, the materials usually react only slowly with water. The use of an acid or alkaline material greatly accelerates the hydrolytic reaction. Thus, in the case of parathion, the rate of hydrolysis is increased many fold by the use of an alkaline material such as sodium hydroxide, sodium carbon, or even lime or calcium carbon. This reaction is shown following:

Hydrolysis



Other types of chemical reactions that may be used for disposal of pesticides include, wet air oxidation, oxidation with permanganate and in the case of the chlorinated hydrocarbons, mild acid reduction with zinc or a zinc copper alloy.

The disposal of pesticides containing metallic elements, such as arsenic, mercury, lead, or cadmium, is difficult because of the persistence of the element. Treatment to form the insoluble sulfide as shown in the reaction below, followed by appropriate disposal can be used.

Sulfide Formation

$$(As^{+5}, Cu^{+2}, Cd^{+2}, Pb^{+2}, Hg^{+2})$$

$$2\,As + 5S \longrightarrow As_2S_5 \text{ (insol)}$$

Methods of Disposal on Land:

There are a number of methods for practices that can be used for disposal of pesticides on land (Lawless et al, 1975; Pollution Control Technology, 1974). Such disposal is often the most convenient and practical where relatively small lots of the chemical are to be dealt with.

Open Pit Disposal. Open pit disposal, by and large, cannot be recommended for pesticides. The opportunity here for air and water contamination is too great.

Landfill. A landfill, that is, a garbage disposal site that is covered can accommodate a very limited amount of chemical. The limitation is on the amount of chemical that may be adsorbed, and thus, prevented from leaching in the groundwater or decomposed in the matrix of garbage. Care should be exercised in siting such a disposal facility, such that neither surface water nor groundwater is likely to become contaminated with the materials disposed in it.

Sanitary Landfill. The sanitary landfill is a disposal site where at the end of each working day, the material disposed of during that day is covered with a layer of soil. The soil layer is then packed by rolling machinery over it to ensure appropriate seals. The sanitary landfill is more suitable for a site of disposal of a limited amount of chemical than the two previously described. The layers of soil provide a site for adsorption of the chemical and restrict leaching, and at the same time there is usually enough microbiological activity to foster the degradation of pesticides. However, if the sanitary landfill is to be used as a place for disposal for a modest amount of chemical, the landfill should be carefully managed. It is taken for granted that such a landfill would be carefully sited away from human habitation and in a place with a suitable geologic formation that there is not the danger of water contamination.

Burying Small Containers and Small Amounts of Pesticides

Special Disposal Sites. Properly managed soil disposal can be a means of getting rid of certain types of chemicals in limited quantities. It is much more effective in disposing of organic chemicals such as many of the pesticides than it is for the inorganic chemicals and heavy metals. The management of such sites utilized a combination of chemical and microbiological means to bring about decomposition of the chemical.

In this type of disposal, relatively small pits are dug to a depth of about one meter. The bottom of the pit is covered with agricultural lime and in the case of a water soluble chemical, charcoal. Should organic matter such as as leaves or grass clippings, or better yet, animal waste be available, they may be added to the pit to enhance breakdown. A limited quantity of the chemical is placed in the pit and covered with a layer of soil followed by additional lime, more of the chemical, and animal waste as available. The pit should not be filled with the chemical nearer than fifteen to twenty centimeters of the soil surface. The pit, then, is covered over with soil and firmly packed. The dimensions of such a pit would be from one to one and a half meters deep by a meter and a half in diameter and contain a limited amount of the chemical. The combination of the lime and organic matter, where it can be added, facilitates the breakdown of such chemicals as the organophosphates, carbamates, amides and triazines. Where suitable animal waste is available in quantity, such pits are even suitable for disposal of small amounts of the organochlorine pesticides. The pits, as described, should be no closer than about six to eight meters apart. Again, it should be on a carefully chosen site to avoid water pollution and should have reasonable security from entry by unauthorized humans.

Soil Biodegradation. Biodegradation in soil is a variation of the disposal method described above. In this instance, rather than burying the chemical in pits, it is distributed over a larger area on and in the soil. This may be done through injection into the soil directly or the material may be sprayed onto the soil and then tilled in. The site chosen for biodegradation should be selected to avoid both surface and groundwater contamination and secured from entry of unauthorized personnel.

Table 15-2. Breakdown of Pesticides in Soil

Type of Pesticide	Time Required for One-half to Break Down in Soil (Days)* Average	Maximum
Organophosphates	47	290
Triazines	82	212
Carbamates	172	817
Arylsubstituted Ureas	355	3103
Chlorinated Hydrocarbons	2256	7987

*Adapted from A. Mercado and Ykahanovitch in "Behavior of Pesticides in Soil," Special Publication #82, Division Sci. Pub. 1977.

The area for biodegradation of the pesticides should be managed much as one would good agricultural land, that is, it should have ample organic matter, received some fertilization, and if necessary, supplemental irrigation. The whole idea of biodegradation is to encourage soil microorganisms and plants to decompose the chemical being disposed of . The site should be maintained as near as possible with a cover of vegetation to prevent wind erosion of any possible contaminated particles. Similarly, there should be drains to intercept any runoff water from the site and carry it into a sump or depression to allow settling of contaminated soil before the water drains off. The sump area should have a vegetative cover, probably some types of low growing grass or broad leaf plants. These serve as a living filter and also help to bring about destruction of the chemical. The whole disposal area, likewise, should have a border of one to one and a half meters wide as a minimum of vegetative area. On a large site, the area could be surrounded by an appropriate hedge row of woody plants with the herbacious border on the inside.

Secure Chemical Disposal Site. For highly toxic chemicals, secure storage and disposal sites are being developed. These sites are dedicated for long period of time as places where the chemicals may be stored in appropriate containers or pits or receive further treatment to increase the safety of the storage. A number of the industrialized countries are turning to such facilities for disposal of toxic waste. At such facilities. limited treatment of the chemicals, such as adsorption on charcoal or resins to reduce the mobility of the chemical, gelation or concretion may be used. A concept behind utiliziing secure areas such as this is that at some future date, it may be economical to recover at least some of the chemical. Such facilities, while assuring safe disposal, are probably most useful to industry and where collection and transport of the chemical does not pose a large problem.

DISPOSAL OF CONTAINERS

Disposal of pesticide containers is quite a consideration. Careless discard of paper or plastic bags can result in a pollution problem, particularly if thrown into ditches, streams, or where the chemical may be leached from such containers into water. Burning is not a satisfactory way of disposing of the paper or plastic bag since the residue of pesticide left in such bags would not burn competely and, therefore, would result in air pollution. If a proper type of incinerator were available, disposal could be in this manner. Burial in sanitary landfills or the type of pits described under "Chemical Disposal," can be used for such bags. Encouraging breakdown through the addition of fertilizer and/or lime as appropriate would accelerate both the degradation of the pesticide and decomposition of the container.

Disposal of glass and plastic jugs or small metal containers poses a somewhat different problem. Often, the bottles or jugs appear to be attractive for other uses. There have been a number of instances of human poisonings where pesticide containers were put to other uses after being emptied of the original pesticide contents. Also, environmental contamination can and has resulted from lack of proper disposal of such containers. Even though such containers can be thoroughly cleaned, in no case should they be recommended for use drinking water or to contain any other item of food. It is probably better to recycle the glass and metal containers either for use with the same pesticide or a similar chemical.

It should be noted that with any pesticide container, whether a small bottle, a jug, or a drum, it is impossible to remove the last traces of the chemical (Lamberton, et al., 1976). When the container is empty, there still may remain from two to ten grams of residual technical material. In drums of larger size there will be proportionally more chemical remaining as a residue. If these residues are allowed to remain in the container for any period of time, they become much more difficult to remove. It is recommended, therefore, that any container for liquid pesticide formulation be rinsed at least three times with water or an appropriate solvent and the rinsings added to the spray mixture. The rinsing should be done immediately after emptying. By this means, as much as 95% - 99% of the residue that would remain without rinsing will be removed. More elaborate treatment for removal of the balance of the residue is possible. In the case of the organophosphate and carbamate insecticides, treatment with a base such as sodium hydroxide or sodium carbonate followed by a detergent rinse and a final soaking with charcoal suspended in the water reduces the residue to a very low or almost negligible level.

For the larger metal containers, drums, barrels and tanks, the best disposal method is to reuse them for the same pesticides. It is becoming more and more economical to return such containers to reconditioning centers to be put back to use. Such reconditioning may involve rinsing with appropriate organic solvent followed by steam cleaning and occasionally chaining to remove the plastic liner followed by relining of the drum. They are then ready to be returned to use. However, such operations must be conducted at appropriate well-equipped facilities.

DISPOSALS OF WASTES ON THE FARM

We have already mentioned the problem of disposal of containers and waste chemical in another connection. Nonetheless disposal of containers and waste chemical is a big enough problem to be worth repeating a few remarks about disposal on the farm (Lawless, et al., 1975). The first step that might be observed by the farmer who wishes to avoid contamination is to make sure that when he empties a container of pesticides, he thoroughly rinse the container before disposing of it (Lamberton, et al., 1976). This serves two purposes, first it reduces the amount of waste pesticide remaining in the container from several mls in a liter container to less than one or two mls of diluted material. If such a container when emptied, is rinsed three times with water and that rinse water added to the sprayer it also means that the farmer is getting all of the chemical that is due him and thus saving money.

Where the containers and waste or surplus chemical must be disposed of on the farm, it is likely one will have to use soil disposal. In this case a site should be selected well away from the house or where animals might get to the disposal, and certainly well away from where it could contaminate water. One method of land disposal consists of a hole dug in the ground to receive the waste chemical and the container to be disposed of. These holes or pits should be about one-half meter deep, maybe something like a meter in diameter and then after the chemical or container has been put into the pit, the whole thing covered over again with the soil that was dug out. It is desirable that lime or calcium carbonate be put into the bottom and along the sides of such a pit if it is available. Carbon or charcoal which is a very good adsorbent for chemicals, may also be used in such pits to ensure that the chemical does not escape. Where large amounts of chemical, or large numbers of containers are to be disposed of, the pits should be larger and by all means the charcoal and lime should be used to help neutralize the chemical. In this case, the pit should be lined with the charcoal and lime, a layer of containers or chemicals added, then a layer of soil followed by more charcoal or lime, additional chemical or containers may be added, but finally the whole thing should be covered over to a depth of not less than 1/4 to 1/3 meter of soil.

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Chapter 16

Registration and Labeling

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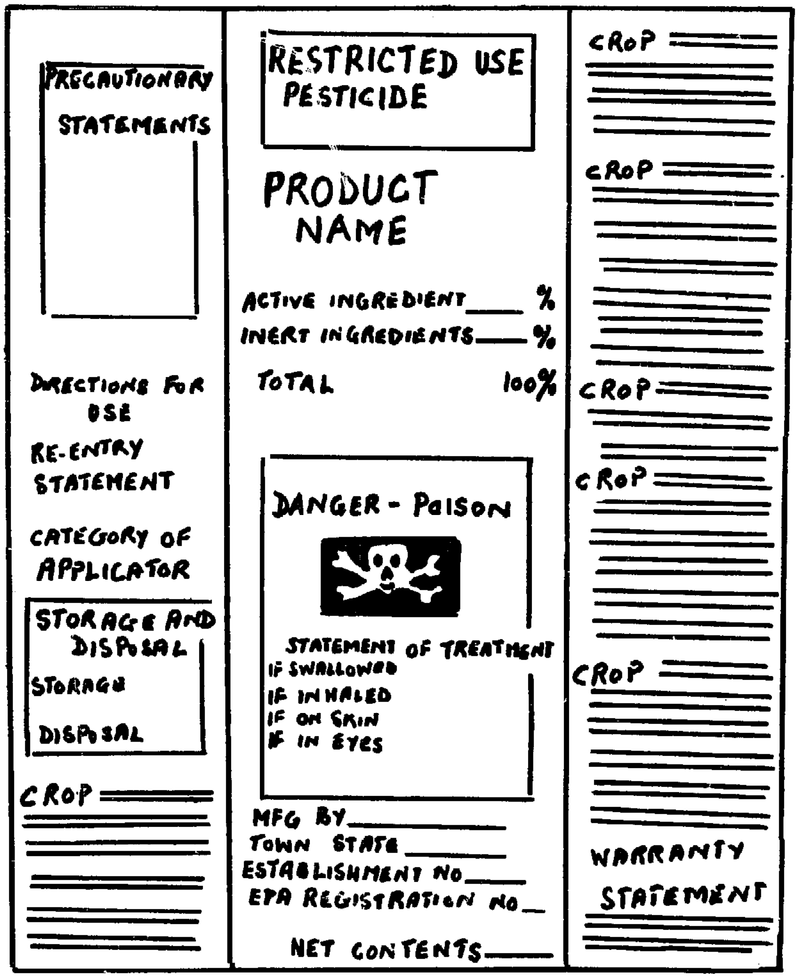

SUMMARY

Registration of pesticides in the developed countries is a highly complex and expensive process requiring large amounts of scientific data, but most data on the fate, movement and effect of pesticides developed in one part of the world can be directly extrapolated to other areas. Where possible, developing countries should expend their major efforts at gaining the non-transferable information and utilize directly, where possible and without substantial modification, those regulatory decisions made in the developed countries.

As a general rule what is not good for a developed country is not good for a developing country. Pesticides which are severely restricted in developed countries on the basis of acute toxicity, if allowed for general use by the small farmer in a developing country, will with a certainty take a heavy toll in lives and physical impairment. Likewise the persistent chlorinated hydrocarbon pesticides, while safe from an acute standpoint, will lead not only to long-term contamination of soil and the aggregate environment but will materially affect the number and diversity of native fish and wildlife species. Additionally, due to their potential for bioaccumulation, the chlorinated pesticides will concentrate over time in certain segments of the environment, including human mothers milk and exert their long-term influence as excessive residues in human body fat.

INTRODUCTION

This chapter suggests approaches for pesticide regulation in the developing countries useful at various levels of economic and social development and how a developing country, at minimum expense, can make maximum use of the regulations already in place within the developed countries. Accordingly this chapter will also attempt to summarize and place into historical perspective the concerns of the developed countries which led to the regulation of pesticides as now practiced in those countries.

Most, if not all, of the developed countries now have highly sophisticated national systems to control pesticides within their country and tracing the legislative history of any of these countries would likely lead to very similar end results. However, with regard to publicly available records, the legislative history of the United States probably offers a unique opportunity to document the underlying rationale for current developed country laws relating to regulation of pesticides. Therefore, the authors will draw freely from the past and current activities from the U.S. with reasonable assurance that the technical procedures and regulatory philosophies used by other developed countries in protecting their individual countrymen and national environments are only superficially at variance with those of the U.S. and are of similar substance. That this is true is confirmed by the recent publication of "Test Guidelines" by the Organization for Economic and Community Development (OECD, 1981) wherein 28 of the developed countries, including the U.S., have by consensus agreed upon mutually acceptable test methodology.

A number of developing countries already have strong pesticide laws on their books but in many cases efforts aimed at enforcing the laws are either negligible or nonexistant. The presence of an adequate law is, however, an important first step in the longer process of adequate regulation of pesticides.

REGISTRATION OF PESTICIDES

Historical

Public concern over pesticides prior to the advent of the synthetic organic pesticides such as DDT, chlordane, heptachlor and dieldrin was minimal. In 1947, shortly after the introduction of the synthetic chlorinated hydrocarbon pesticides, the U. S. passed the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA, 1947), which required:

1. The registration of economic poisons or chemical pesticides prior to their sale or movement,
2. The prominent display of poison warnings on labels of highly toxic pesticides,
3. The coloring or discoloring of dangerous white powdered insecticides to prevent their being mistaken as foodstuffs,
4. The inclusion of warning statements on the label to prevent injury to people, animals and plants, and
5. The inclusion of instructions for use to provide adequate protection for the public.

This law gave the government substantial authority in terms of requiring the careful and explicit labeling of pesticides as to their contents, use and hazard. It did not, however, allow for removal of chemicals from the market place regardless of their danger. Also, little provision was made for data requirements to demonstrate the safety of the chemical.

This Act was materially strengthened in 1954 by passage of an Amendment to the Food, Drug and Cosmetic Act (FDA, 1954) requiring the establishment of "tolerances" for chemicals in or on agricultural commodities.

It also authorized the requirement for scientific data to prove safety of the chemical when used as directed.

Increased concern over the effects of pesticides was stimulated by the book "Silent Spring" (Carson, 1962) which along with the results of federally funded environmental monitoring studies (USDA, 1966) and an advisory group report on the potential health hazards of pesticides (Mrak, 1969) culminated in 1970 with the formation of the Environmental Protection Agency and the passage of a major amendment to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA, 1972). In addition to increasing the government's enforcement powers, this new law introduced the "benefit-risk" concept wherein the economic, social and environmental costs and benefits for a pesticide could be taken into account in defining what are "unreasonable adverse effects on the environment."

This law further required that all pesticides be classified for general or restricted use depending upon their effect on man and the environment and provided for the training and certification of applicators of restricted use pesticides after exhibiting a satisfactory knowledge and ability to safely apply pesticides. During the 1970s much of the regulatory activity in the developed countries has surrounded the development, evaluation and adaptation of chemical and biological testing procedures for safety evaluation to human, fish and wildlife and environmental aspects of pesticide registration. Much of the current controversy in the area of pesticides involves not the newer pesticide chemicals but whether or not the criteria and testing procedures by which older chemicals were formerly registered should still be accepted in view of more recent findings on the inadequacy of certain of the older testing procedures.

The remainder of this chapter deals with reviewing the current status of pesticide regulatory activities in the developed countries along with suggestions as to how these can be used with maximum utility at minimum expense to the developing country.

Guidance for drafting pesticide legislation in developing countries

The Food and Agriculture Organization (FAO, 1969), in recognition of a widespread need for such legislation developed a set of "Guidelines Concerning the Sale and Marketing of Pesticides." These guidelines, in spite of their age, are still highly relevant to developing country needs and are an excellent starting point for development of national laws tailored to individual country needs. Additionally, the U.S. Federal Insecticide, Fungicide and Rodenticide Act, as amended (FIFRA, 1978) provides a comprehensive overview of almost all conceivable aspects of pesticide legislation which could in the near future ever be needed by any country in forming legislation.

By judicious elimination of certain sections and subsections of the FIFRA (which would not be relevant to a developing country's need) an Act could be developed which with little or no modification would be in consonance with the 1969 FAO guidelines and which could serve as the basis for the building of any needed regulatory infrastructure.

As stated earlier, the existence of a pesticide law is only a first step (albeit an important step!) in the longer process of effective regulation of pesticides. A forthcoming document (Compendium, 1982) will outline the pesticide laws of over 80 different countries. However, it is highly doubtful if more than one third of these countries have effective pesticide regulatory infrastructures. Table 16-1 illustrates the great variability of the status of pesticide regulation and enforcement in the Caribbean countries in 1981.

Guidance for implementation of a pesticide law

Existence of a pesticide law without accompanying regulations for enforcement and personnel to accomplish such enforcement of a pesticide law is obviously of little utility. An excellent example of the form such regulations can take is given in the "final" rules as codified in the U.S. Federal Register (CFR, 1981) related to pesticide regulation in the U.S. In addition to general registration procedures these regulations provide for: procedures and standards relating to licensing of pesticide applicators, disposal and storage of excess pesticides and containers, issuance of experimental use permits, classification procedures, rules of practice governing legal hearings related to classification, cancellation or suspension, farm worker protection standards, conditional registration and registration of establishments. A careful review of these regulations is highly instructive as to how a relatively simply worded law (FIFRA, 1978) can be interpreted in the form of rules and regulations useful for day to day enforcement of the law.

FAO has published a "Model Scheme for the Establishement of a National Organization for the Official Control of Pesticides" (FAO, 1970). This document proposes a scheme whereby up to six stages can be implemented in a sequential order. The simplest form of the scheme as proposed is based on appointing a director of the organization. As funds allow, supporting staff can be added in stages by the staffing of various sections dealing with specific topics. A definite order of expansion is suggested, but it does not follow that the proposed order will best suit the needs of all countries and it may be necessary in many cases to rearrange the order of expansion.

The simplest form of the proposed scheme would be the appointment of a Director of a Pesticide Control Committee. This Director would chair one or more advisory committees each having separate advisory panels to cover various important subspecialties. For example, an advisory committee on pesticides safety would utilize the assistance of special panels on wildlife protection, toxicity and user hazards, residue analysis, etc. Although not stated it is assumed that in the simplest of circumstances, the Director would be a paid employee of the government and the members of the advisory committee would serve in a voluntary capacity with their time being donated by their employers as a form of civic involvement.

Table 16-1. Status of Pesticide Laws and Regulations and Enforcement in the Caribbean countries, 1981.

Country	Pesticide Act	Status of Pesticide Regulations
Trinidad/Tobago	Pesticide and Toxic Chemicals Act, 1979	In process of being drafted by PTC Act Board but not yet enforced
Jamaica	Pesticide Control Act, 1975; amended 1977 but not gazetted	Regulations not yet formulated
Barbados	Pesticide Act, 1973; Pesticide Control Regulations, 1974 and Labeling, 1976	Partial enforcement
Grenada	Pesticide Act No. 28, 1973; Regulations for Control, 1979	Enacted and enforced
Dominica	Pesicide Control Law enacted, regulations on registration, labeling, etc.	Promulgated but not enforced
Guyana	No act	Draft regulations in place Food & Drug act is complimentary
St. Vincent	Pesticide Act, 1973	Regulations not promulgated or enforced
St. Kitt	Pesticide Act No. 20, 1973	Pesticide Board formed and regulations promulgated 1975
St. Lucia	Pesticide Control Act law enacted on registration, labeling, etc.	Promulgated but not enforced
Antigua	No Act	Regulations drafted but not enforced
Bahamas	No Act	No regulations
Belize	No Act	Pesticide Control Committee formed 1975, not enforced
Haiti	No act	No control board
Dominican Republic	Pesticide Law, 1971 Regulation #1390	Promulgated and enforced

Davies, 1981

The other stages of the model scheme are listed below:

Stage II - (Laboratory Quality Control)
Stage III - (Evaluation of Efficacy)
Stage IV - (Residue Control)
Stage V - (Evaluation of User and Third Party Hazards)
Stage VI - (Evaluation of Toxicological Hazards)

Types of data normally required for registration of a pesticide

Currently the cost of registering a new pesticide for a food use in the U.S. can be up to $20 million dollars. Most of these costs are directly related to developing scientific data on the chemical's safety. In addition, of course, the chemical must be proven effective for the use intended.

General

The general data requirements to establish the safety of a pesticide have been published (EPA, 1978, 1978a, 1980; FAO, 1981; OECD, 1981) and include toxicology, product chemistry, environmental chemistry and fish and wildlife requirements. Each of these type data requirements is discussed in more detail below.

Product chemistry studies (EPA, 1980)

Data on physical and chemical properties are required for all pesticides regardless of whether they are technical grade, manufacturing use product or formulated product. Tests required for one or more of these product types include: color, odor, physical state, melting point, boiling point, specific gravity, solubility, vapor pressure, dissociation constant, octanol/water partition coefficient, pH, storage stability, viscosity, miscibility and flammability.

Also, analytical methods useful for verifying the certified ingredient limits are required, including impurities which show up in amounts of 0.1% or greater.

In addition tests have been proposed for detecting the presence of potentially genotoxic ingredients present at levels of less than 0.1%.

Toxicology studies (EPA, 1978)

The following studies are generally required for pesticides which are to be used for food or feed crops. For non-food uses, fewer tests are required:

1. Acute and subchronic oral and dermal toxicity studies
2. Chronic two year feeding studies
3. Mutagenicity, oncogenicity, reproduction and teratogenicity studies

Environmental Fate Studies (EPA, 1978a)

The following types of studies relating to prediction of the ultimate environmental fate of a pesticide are required of all products used for out-of-doors agricultural uses:

1. Degradation (Hydrolysis, photolysis, field dissipation, metabolism)

2. Mobility
3. Residue accumulation

Food Residue Studies (FAO, 1981)

Residue studies as needed in support of a tolerance are required by all developed countries. An excellent guideline published by the FAO gives a thorough description of sampling procedures and related information.

Environmental Effect Studies (EPA, 1980)

Requirements for effects of pesticides on wildlife and aquatic organisms include the determination of LD_{50} value as well as include chronic and subchronic exposure studies, to determine the effect of pesticides on reproduction.

Efficacy

In addition to safety information, data are required to substantiate efficacy claims made for the pesticide product. Evidence of product efficacy must be demonstrated through laboratory and/or field testing procedures which simulate actual use conditions.

Positive Steps at Pesticide Regulation Which Can Be Taken by a Developing Country With Minimal Pesticide Regulatory Infrastructure

Control of Toxicity Category I pesticides

In much of the developed world certain pesticides are considered to be too toxic for general use. In the U.S., after a long history of many fatal poisonings the pesticide laws were changed so that the more highly toxic pesticides were placed in a special RESTRICTED category. Pesticides in Toxicity Category I (see Table 16-2 below) are classified as RESTRICTED and can only be sold to certified applicators.

Table 16-2.	Toxicity categories			
Hazard indicators	I	II	III	IV
Oral LD_{50}	Up to and including 50 mg/kg	From 50 thru 500 mg/kg	From 500 thru 5000 mg/kg	Greater than 5000 mg/kg
Inhalation LD_{50}	Up to and including .2 mg/liter	From .2 thru 2 mg/liter	From 2. thru 20 mg/liter	Greater than 20 mg/liter
Dermal LD_{50}	Up to and including 200 mg/kg	From 200 thru 2000 mg/kg	From 2000 thru 20,000 mg/kg	Greater than 20,000 mg/kg
Eye effects	Corrosive; Corneal opacity not reversible within 7 days.	Corneal opacity reversible within 7 days; irritation persisting for 7 days.	No corneal opacity; irritation reversible within 7 days.	No irritation
Skin effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours

In order to be certified, applicators need to receive special training as well as agree to wear protective clothing when applying the pesticides. Most of the accidental fatalities caused by pesticides in both the developed and developed nations are caused by pesticides in Toxicity Category I.

While not universally true most pesticide-use patterns involving Toxicity Category I pesticides can be effectively substituted by pesticides in a lower toxicity category. A notable exception to this is cotton culture where excessive misuse of pesticides over the years had led to severe resistance problems. Most other developing country agricultural pest control practicies have not involved such pesticide misuses that Category I pesticides have become essential.

A very effective mechanism for regulating Toxicity Category I pesticides would be to prohibit their import into the country unless a true need, not capable of resolution by substitution of a less toxic pesticide, could be shown. In those rare cases where a bona fide need was demonstrated the importer (or distributor) could be held responsible for distribution of the pesticide and training of the affected agriculturists. Import permits could be tightly controlled to only allow treatment of a predetermined acreage of a specific crop and crop pest complex. Any widespread unauthorized sale or use could be cause for revocation of the limited import permit and recall of existing stocks at importer expense.

A partial list of Toxicity Category I Pesticides is shown in Table 16-3.

Table 16-3. Toxicity Category I Pesticides
(Based on oral, dermal or inhalation hazard)

---

acrolein
acrylonitrile
Actidione®
Agritox®
aldicarb (Temik®)
aldoxycarb
allyl alcohol
aluminum phosphide (Phostoxin®)
aminocarb (Matacil®)
Amaze®
4-aminopyridine
Avitrol®
azinphos-ethyl (ethyl Guthion®)
azinphos-methyl (Guthion®)
Azodrin®
Bidrin®
Birlane®
Bladafume®
bromophos-ethyl
bromsalans (Diaphene®)
bomyl (Swat®)
bromadiolene (Maki®; Ratimus®)
calcium cyanide
Carbicron®
carbofuran (Furadan® all liquid formulations)
carbon disulfide
carbon tetrachloride
carbophenothion (Trithion®)
Carzol®
Castrix®
Celathion®
chlormephos (Dotan®)
chlorfenvinphos (Birlane®; Supona®)
chloropicrin
chlorthiophos (Celathion®)
Compound 1080
copper acetoarsenite
coumafuryl (Fumarin®)
Counter®
crimidine (Castrix®)
Curaterr®
cyanophenphos (Surecide®)
cyanthoate (Tartan®)
Cyolane®
Cytrolane®
Dasanit®
Delnav®
demeton (Systox®)
demeton-s-methyl (Metasystox®)

Table 16-3. (continued)

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dialifor (Torak®)
Diaphene®
dicrotophos (Bidrin®; Carbicron®; Ektafos®)
dieldrin
Dimecron®
dimefox
dimethrin
dinitrophenol
dioxathion (Delnav®)
disulfoton (Disyston®)
dinitro-o-cresol (DNOC)
Disyston®
DNOC (dinitro-o-cresol)
Dotan® (chlormephos)
Dyfonate®
Ekatfos®
endothall
endrin
EPN
ethyl Guthion®
ethoprop (Mocap® liquid formulations)
famphur
Fac®
fenamiphos (Nemacur® liquid formulations)
fenamisulf (Lesan®)
fensulfothion (Dasanit®)
Fentin chloride
fluenyl (fluenethyl)
fluoroacetanilide
fluoroacetamide
Folimat®
fonofos (Dyfonate®) all liquid formulations greater than 40%
formetanate hydrochloride (Carzol®)
fosthietan (Nematak®)
fonophos (Dyfonate®)
Fumarin®
Furadin® (Carbofuran) all liquid formulations
Gophacide®
Guthion®
izofenphos (Amaze®)
Lannate® (Methomyl)
Lesan®
Maki®
Matacil®
mecarbam
mephosfolan (Cytrolane®)
mercaptodimethur (Mesurol®)
mercury chemicals (all known types)
Mesurol®
Metasystox®
Methamidiphos (Monitor®)
methidathion (Supracide®)

Table 16-3. (continued)

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methiocarb (Mesurol®)
methomyl (Lannate®) all formulations
    not packaged in water soluble bags
methyl bromide
methylene dibromide
methyl parathion
mevinphos (Phosdrin®)
Mocap®
monocrotophos (Azodrin®)
Monitor
Nemacur®
Nem-a-tak®
Nexagan®
nicotine
omethoate (Folimat®)
oxamyl (Vydate®) liquid formulations
oxydisulfoton (Disyston-S®)
Panogen® a very dangerous mercury containing chemical
parathion
phorate (Thimet®)
phorazetim (Gophacide®)
Phosdrin®
phosfolan (Cyolane®)
phosphamidon (Dimecron®)
Phostoxin®
potasan
Previcur-N®
propamobcarb hydrochloride (Previcur-N®)
prothoate (Fac®)
Ratimus®
schradan
scillirosid
sodium arsenite
sodium cyanide
sodium monofluoracetate (Compound 1080)
sulfotepp (Bladafume®)
strychnine
Supona®
Supracide®
Surecide®
Swat®
Systox®
Tartan®
Temik®
1080
TEPP
terbufos (Counter®)
thallium sulfate
thionazin
Torak®
triamiphos (Wepsyn 155®)
trichloronate (Agritox®)
Vydate®
Wepsyn 155®
zinc phosphide

Control of Suspended, Cancelled and Withdrawn Pesticides

Most uses of the chlorinated hydrocarbons for agricultural purposes have been suspended in the developed countries. Heptachlor, Mirex®, Kepone®, endrin, chlordane, BHC, DDT, aldrin, and dieldrin have all been severly restricted and none of them have registrations for food crop production uses. All of these pesticides are chlorinated hydrocarbons, highly persistent and can accumulate in the environment. Many of them enter the food chain and are bioaccumulative during their passage through successive steps in the food chains (EPA, 1979; Edwards, 1973).

Since safe and effective substitutes for the chlorinated hydrocarbons exist for all known food pest uses, an outright ban on all importation except for public health uses is entirely feasible.

In addition several other pesticides are no longer marketed in most developed countries due to adverse toxicological findings or their use has been severely restricted. A listing of pesticides which have been the subject of such considerations is shown below in Table 16-4.

Table 16-4. List of Cancelled, Suspended, Withdrawn or Specially Regulated Pesticides

silvex (most uses)
TOK® (nitrofen)
2,4,5-T (most uses)
DBCP (Nemagon®) (dibromochloropropane)
chlordimeform (only can be used in closed systems) also called Galecron®
Gardona®
chlorobenzilate
paraquat (use is RESTRICTED due to human toxicological properties and history of accidental poisonings) also called Grammoxone®
aldrin
leptophos
Mirex®
DDT
chlordane
BHC
dieldrin

hexachlorobenzene
Perthane®
Kepone®
heptachlor
heptachlor epoxide
endrin
all mercury containing chemicals

Utilization of registration information from developed countries

Full scale implementation of a pesticide registration program is a costly effort. In the U.S., the Office of Pesticides of the Environmental Protection Agency (EPA) currently employs over 600 people and has an annual operating budget of $60,000,000. Hundreds of other employees in other sections of EPA and within other governmental departments also devote full time effort to pesticide related research and monitoring efforts. Smaller, but substantial investments in pesticide regulatory infrastructures also exist in the United Kingdom, Canada, Australia, W. Germany, The Netherlands, Switzerland and Japan. All of the above have rigorous data requirements with regard to human and environmental safety and all specify a maximum permissible level of any pesticide allowed for in foods within their countries. These allowable levels are usually given the term "tolerances."

Another term which is important in terms of a pesticide safety is that called the "ADI." An ADI is an allowable daily intake level (expressed as mg/kg of body weight) which on the basis of all the known facts appears to be without risk during a lifetime. The ADI is usually based on dividing the value of the no observable effect level (NOEL) as determined in long-term animal feeding studies, by a safety factor to take into account species variability and other unknown factors.

ADIs for over 120 pesticide chemicals have been recommended by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR, 1980). This activity, jointly sponsored by the Food and Agriculture Organization and the World Health Organization consists of two expert groups, one of toxicologists and one of pesticide residue chemists, who meet annually both in separate and joint session. The group of toxicologists meets to develop recommendations for ADIs based on toxicological data supplied the various pesticide manufacturers. Unfortunately many pesticides currently in active use in many LDCs are not covered by such ADIs.

Tolerances are the maximum residue levels which can legally remain in or on food and feed in commerce. They are stated in units of milligrams of pesticide (and/or toxicologically significant metabolites) per kg of food or feed. Before a pesticide is registered for use on a food or feed crop in any of the above mentioned countries a tolerance is established on at least one agricultural commodity. Data submitted in support of a tolerance always is expected to include detailed information on the amount, frequency and timing of pesticide application as well as details on the method of application and the type of formulation used. At least 15 countries have established tolerances for pesticides permitted for use within their borders (Bennet, 1979). The European Common Market also has established tolerance levels for products traded between member countries and an international system of tolerances entitled maximum residue levels (MRLs) has been established by the Joint Meeting on Pesticide Residues of the WHO/ FAO (JMPR, 1980). From a purely legal standpoint a tolerance (or MRL) is no more nor no less than a legal upper limit, which if exceeded can result in action by regulatory authorities.

The MRLs as set by JMPR are set on the basis that "good agricultural practices" are being followed. However, when residue data are reviewed by that group from different areas of the world the actual agricultural practices as well as the climatic conditions are highly varied. This in turn can lead to widely divergent residue levels between geographic areas at the time of harvest. When an MRL is set it is always set at the maximum expected level consistent with "good agricultural practices" regardless of the amount of residue data substantially below this level. In most but not all cases the specific "good agricultural practice(s)" utilized in setting the MRLs are published in the Monographs (FAO, 1967 et seq).

These Monographs are technical reviews of the chemical, physical, toxicological and environmental properties of the active pesticide ingredient based on information supplied by the basic manufacturers. Formal international acceptance of MRLs, as proposed by the FAO/WHO Joint Meeting on Pesticide Residues is done through the Codex Committee on Pesticide Residues of the Codex Alimentarius Commission (Codex, 1978). Tolerances in the U.S. are always originally set on the basis of a specific recommended usage. This recommended usage involves following well defined procedures of formulation, dose rate, application frequencies and timing of last application prior to harvest. Subsequent applications for registrations of the same pesticide, if different substantially in type of formulation or pattern of use, require submission of additional data showing that the original tolerance will not be exceeded.

These U.S. tolerances are currently set based on consideration of both the ADI and the daily food intake. Consideration of both the "average" and the actual food intake are considered necessary since it is generally accepted that the lifetime "average" underestimates the exposure for people who consume more than the "average" quantity of food.

It is important to recognize that in most cases the actual level of residue found in food, as consumed, is substantially lower than that of the established tolerance.

Countries which exert rigorous controls over pesticide use within their borders include: the U.S., W. Germany, Japan, Switzerland, the Netherlands, the United Kingdom, Canada and Australia. As a general rule a pesticide use pattern approved in one of these above mentioned developed countries would offer the same relative degree of risk in a developing country. *However, as the patterns of use in the developed and developing countries diverge, the potential for relative risk differences increases!* Any pesticide from a developed country which has a *bona fide* tolerance in the country of manufacture can be presumed to have reached an advanced state of toxicological evaluation. In order for a tolerance to have been set an acceptable daily intake (ADI) would need to have been established and this ADI in turn would normally be based on adequate toxicological data.

The existence of an ADI in at least one of the aforementioned developed countries or as recommended by the FAO/WHO is a critical item for consideration by a developing country wishing to import and use a new pesticide chemical for food crop uses. In the absence of such an ADI, the developing country considering the registration of a new pesticide would, in most instances, be correct in assuming that the pesticide product either has not passed or could not pass the current safety screening procedures as used in the developed countries.

Sometimes in the U.S. the ADI of a chemical is not a matter of public record. Instead tolerances for the chemical may be issued until the additive typical dietary intake of the several food items reaches a level where the ADI intake is approached and where issuance of another tolerance would cause the ADI to be exceeded under "typical" dietary conditions. In the absence of an ADI the developing country can estimate a hypothetical value by multiplying the average dietary intake of each food item in kilograms by the established tolerance (in mg. of pesticide/kg. of food item) and summing these products for the various food items. When this approach is taken it is important that the final result be reported in the standard ADI units of mg of pesticide/kg of body weight. For an adult a value of 60 kg is usually used.

In the absence of either tolerance or ADI information the toxicological safety of the chemical should be highly suspect and any decision to allow the use of the chemical should only be made after dialog with the manufacfacturer and careful review of all data.

With the large number of pesticides of all types which now carry ADIs, tolerances and developed country use patterns the need to accept new chemicals with questionable or untested safety aspects should be very infrequent and only considered under exceptional circumstances. If a true emergency exists (or appears to exist) a temporary license to import the new product should be granted and strict controls on the quantity of product allowed should be imposed. <u>The product should be limited to an amount needed to treat the known acreage of crop in danger for a single season</u>.

As stated on page 249 a mechanism exists whereby review of such cases by an expert body can sometimes be undertaken on request of the official governmental body responsible for pesticide regulation.

Much of the above discussion relating to the use of registration information from the developed countries relates to pesticide uses on food and the significance of residues in the raw agricultural commodity produced with the aid of pesticides. Another consideration of equal importance, but only recently given emphasis, even in the developed nations, is that of farm worker exposure to pesticides during the course of actual application to the crop or field. That such exposure takes place is well documented and its significance cannot be discounted. Further discussions on this route of exposure can be found in Chapter 10.

LABELING OF PESTICIDE PRODUCTS

An extremely important aspect of regulation of pesticides is the requirement for labeling. Pesticide labels are the most important means of communication between the user, the regulator and the pesticide manufacturer. The label provides the information indicating the nature of the pesticide, how it is to be used, the percentage of active ingredient, and the precautions to take in using the material. It is important that the label be in language or symbols that is understandable by the user. Information on the label represents the summation of years of research on the safety and effectiveness of the pesticide formulation. It is one of the most useful and authentic documents on the chemical available. The label, therefore, should contain at the very least, the following information (Refer to Figure 16-1):

A. <u>Product Name</u>, Brand Name or Trademark
This name should not give misleading impression as to contents or their activity and should make no false representation.

B. <u>Common and Chemical Name</u>
Most pesticides have common names established by one or more of the following standards setting organizations; K62 Committee of the American National Standards Institute, Inc; British Standards Organization, International Standards Organization. Chemical names for new active ingredients are routinely established by the Chemical Abstracts Service of the American Chemical Society. A recent listing of common and chemical names for most pesticides has been published by the USEPA (EPA, 1979a).

C. Percentage of Active and Inert Ingredients

In all cases the total of both active and inert ingredients must add up to 100%.

D. Net Contents

The weight or measure stated should be accurate as to quantity and should not vary below the claimed quantity. Unreasonable variations above the claimed quantity should also be prohibited. The units of measure should be in metric units as well as those in local use.

E. Name and Address of Manufacturer, Packager, Producer or Registrant

The label should be that of the manufacturer or should be qualified to show that the name is not the manufacturer. For example, "Distributed by," Packed for," "Sold by."

F. Registration Number for the Product

In addition to product registration numbers the number of the establishment in which the formulation is actually produced is sometimes also added. Also, a production batch number is sometimes added so that in the event of an emergency recall of the chemical only those batches having specific numbers need be removed from distribution centers, stores, warehouses, etc.

G. Safety Symbols, Signal Words or Other Indication of Toxicity to Humans

Appropriate wording to warn the user of the product as to danger from toxicity is needed. In some parts of the world, the skull and crossbones along with the word "POISON" is used for the most toxic materials. Sometimes a color (e.g., red) connotes danger within a certain cultural context. If so, such a color could be reserved for more highly toxic chemicals. For example, the word POISON in large red letters agains a white background is a very effective warning symbol in many parts of the developed world. The signal words "Danger," "Warning" and "Caution" are used in the U.S. to denote three different orders of toxicity.

Signal Words	Toxicity	Approximate Amount Needed to Kill the Average Person
DANGER	High	A taste to a teaspoon
WARNING	Moderate	A teaspoon to a tablespoon
CAUTION	Low	An ounce to more than a pint

H. Statement of Practical Treatment

Emergency first aid procedure and information for physicians on the treatment of poisonings, including antidotes.

I. Physical and Chemical Hazards

Any special fire, chemical or explosion hazards should be summarized along with necessary precautions.

J. Directions for Use

In addition to mixing instructions the rate, number, frequency and timing of applications should be stated. If special equipment is needed to apply the pesticide it should be described and if field re-

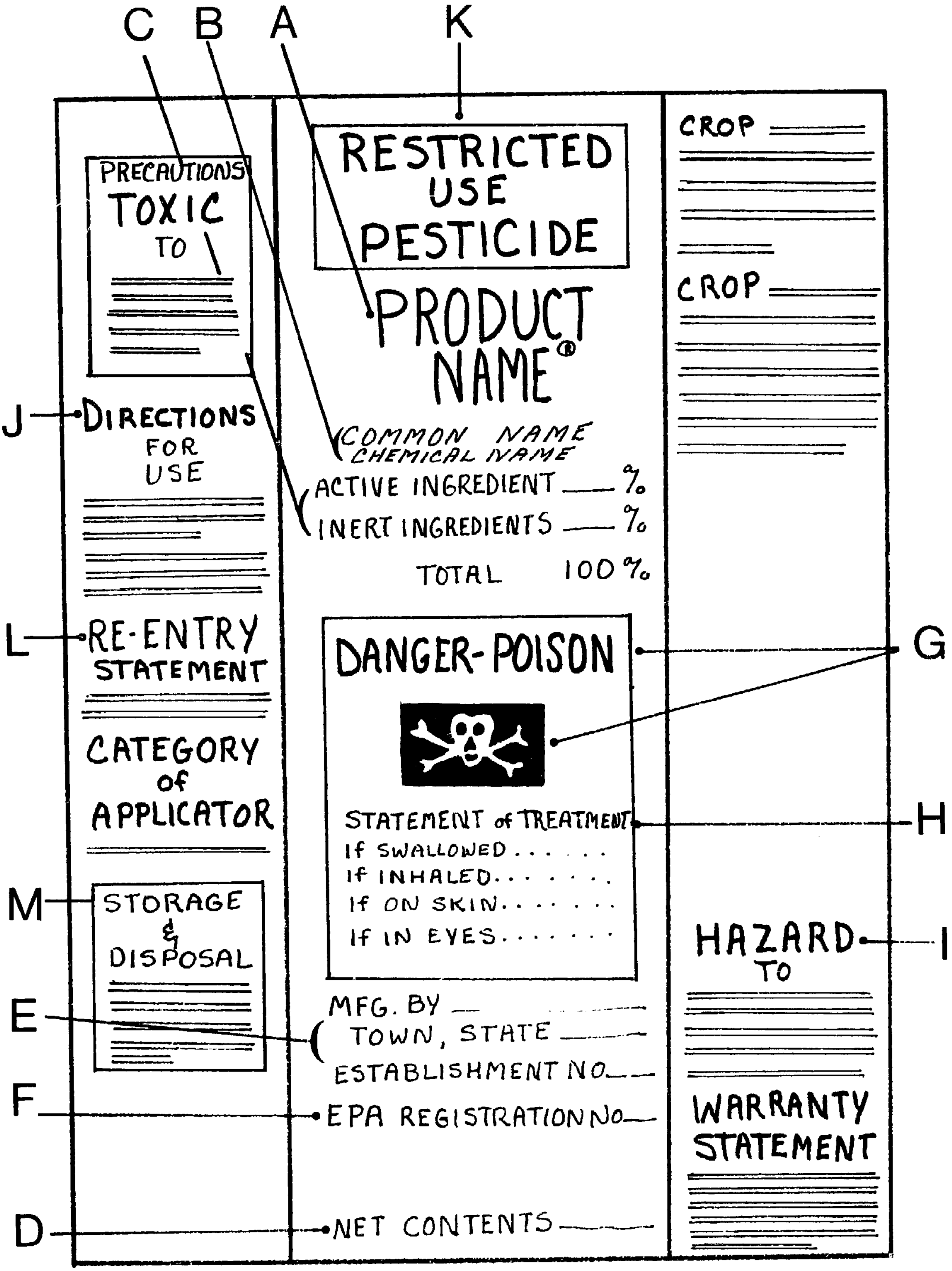
C
B
A
K
PRECAUTIONS
TOXIC TO
RESTRICTED USE PESTICIDE
PRODUCT NAME®
CROP
CROP
J
DIRECTIONS FOR USE
COMMON NAME
CHEMICAL NAME
ACTIVE INGREDIENT ___ %
INERT INGREDIENTS ___ %
TOTAL 100 %
L
RE-ENTRY STATEMENT
DANGER-POISON
G
CATEGORY of APPLICATOR
STATEMENT of TREATMENT
H
If SWALLOWED
If INHALED
If ON SKIN
If IN EYES
M
STORAGE & DISPOSAL
HAZARD TO
I
E
MFG. BY
TOWN, STATE
ESTABLISHMENT NO.
F
EPA REGISTRATION NO.
WARRANTY STATEMENT
D
NET CONTENTS

Figure 16-1.

entry times are involved they should be stated. The label should clearly state the interval between last treatment and harvest upon which the tolerance is based.

K. Classification Status

As stated earlier, if a pesticide formulation is in Toxicity Category I it should not be sold for general use. In the hands of untrained workers and without special precautions related to protective clothing, poisoning with these chemicals is a virtual certainty. Any distribution and marketing of such chemicals should only be done under carefully controlled and monitored conditions. Such pesticides should be classified as RESTRICTED USE ONLY and this restriction should be made part of the label statement. Control over the manufacture, import, distribution, packaging and sale of such pesticides along with maintenance of appropriate records is best done by issuance of revokable licenses to these various groups.

L. Precautionary Statements

If the pesticide is specially toxic to any form of fish or wildlife the label should so state and any special precautions needed to protect the environment should also be included. Also if there is an interval between treatment of a field and time that a worker can reenter the field it should be stated here.

M. Storage and Disposal

Any special precautions with regard to storage, shelf life and disposal directions for empty containers should be clearly stated.

N. Collateral Labeling Information

In cases where Directions for Use require more space than can be easily contained on the label to be affixed to the pesticide container, a collateral data sheet should be used. However, under no circumstances should the primary label be deprived of any of the other items of information described above. The allowance of collateral labeling should be kept to a minimum and should be the exception rather than the rule.

The need for continuing review of a product's safety in the light of new findings

The registration process involving pesticides is a dynamic one and existing registrations must be reviewed from time to time to determine whether they are still acceptable in the light of current knowledge. One such review process, as used in the U.S., places emphasis on certain risk criteria of the chemical. If none of the various risk criteria are encountered the registration of the chemical would be continued or renewed as the case may be. A summary of the risk criteria follows:

Acute Toxicity:

1. Hazard to humans and domestic animals.
   a. Has an acute dermal LD_{50} of 40 mg/kg or less as formulated; or
   b. Has an acute dermal LD_{50} of 6 oz/kg or less as diluted for use in the form of a dust or spray.

   c. Has an inhalation LC_{50} of 0.04 mg/liter or less as formulated.

2. Hazard to wildlife.

   a. Occurs as a residue immediately following application in or on the feed of a mammalian species representative of the species likely to be exposed to such feed in amounts equivalent to the average daily intake of such representative species, at levels equal to or greater than the acute oral LD_{50} measured in mammalian test animals as specified in the Registration Guidelines.

   b. Occurs as a residue immediately following application in or on avian feed of an avian species, representative of the species likely to be exposed to such feed in amounts equivalent to the average daily intake of such representative species, at levels equal to or greater than the subacute dietary LC_{50} measured in avian test animals as specified in the Registration Guidelines.

   c. Results in a maximum calculated concentration following direct application to a 6-inch layer of water more than 1/2 the acute LC_{50} for aquatic organisms likely to be exposed as measured on test animals specified in the Registration Guidelines.

Chronic Toxicity:

1. Induces oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation or dermal exposure; or induces mutagenic effects, as determined by multitest evidence.

2. Produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator of EPA, which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety; or

3. Can reasonably be anticipated to result in significant local, regional, or national population reductions in non-target organisms, or fatality to members of endangered species.

Developed Country Policies with Regard to Exports of Pesticides to Developing Countries.

Most major developed countries are exporting pesticides to developing countries and it is well known that these include chemicals which are not permitted for general use in the country of origin. There are many arguments pro and con as to whether these current practices are satisfactory but, since this chapter is intended to serve primarily as a guide to regulation at and within the borders of developing countries they will not be discussed here. The current policy in use by the U.S. is summarized below:

> Pesticides, devices and active ingredients covered by Section 17(a) of FIFRA used in producing pesticides for export must now bear certain

minimal labeling. In addition, pesticides covered by Section 17(a) cannot be lawfully exported, unless prior to export, (1) the foreign purchaser has signed a statement acknowledging that the purchaser is aware that the pesticide is not registered in the United States, and (2) a copy of that statement has been submitted to EPA by the exporter for transmittal to the appropriate officials of the importing country. The foreign purchaser acknowledgement statement must accompany the first shipment of each unregistered pesticide to a particular purchaser for each importing country, annually.

PACKAGING

Proper packaging of pesticides is crucial in protecting the health of the consumer as well as those involved with the distribution, handling and sale of the product. Guidelines suitable for establishing a regulatory policy on packaging can be found (FAO, 1982 and UNIDO, 1982).

Some excellent discussion on packages and packaging practices can be also found in recent international regulations for the shipment of hazardous materials by air (ICAO, 1982).

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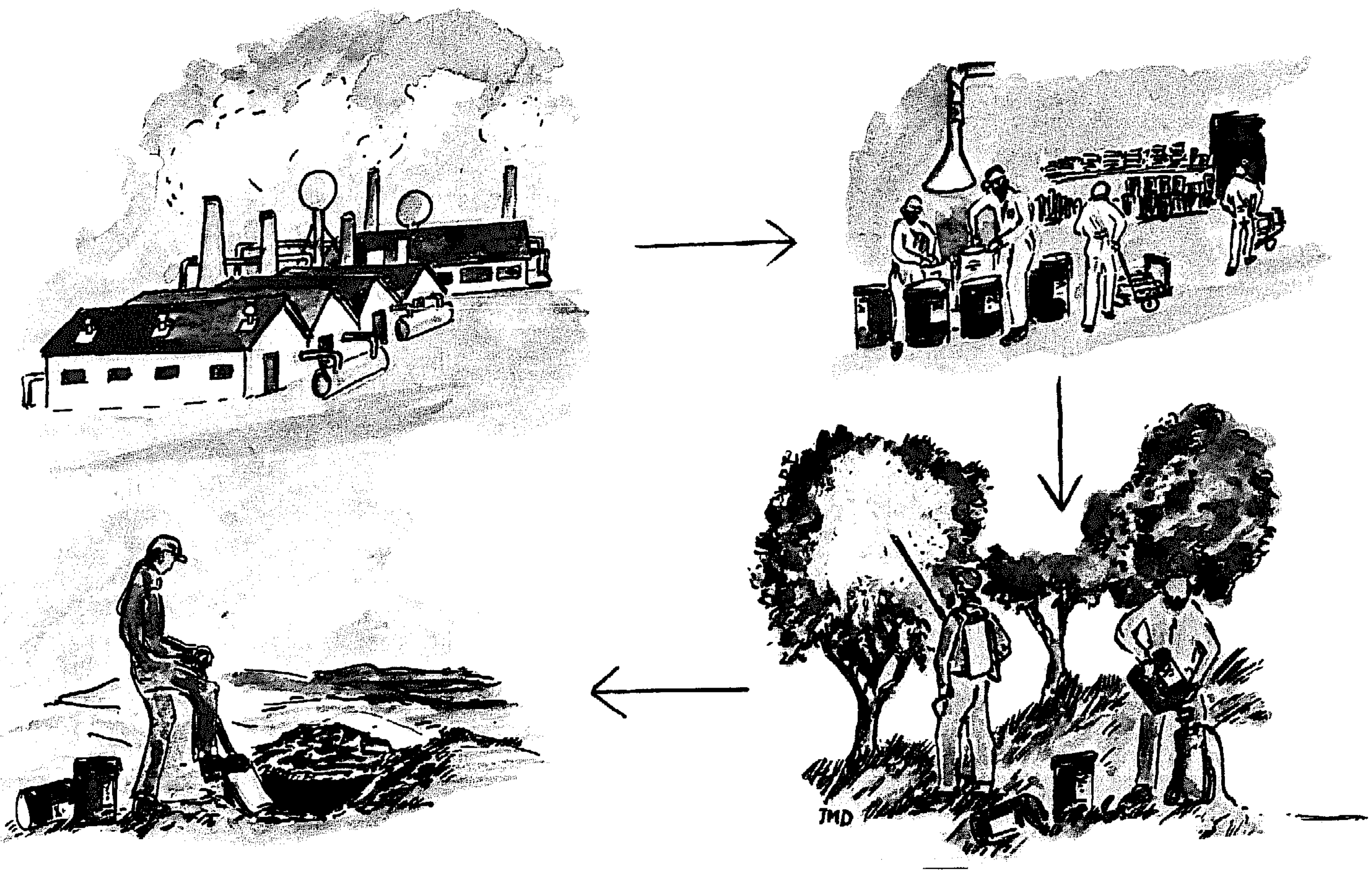
Chapter 17

Reduction of Pollution

Freed, V.H.



SUMMARY

In the flow of a pesticide through the channels of commerce from manufacture to use and disposal there are many instances where pollution can occur. Proper handling, good management and use of pollution control techniques can substantially reduce the pollution problem. Such techniques as vegetative borders, carbon filters and liquid extractors of simple design have proven both economic and effective.

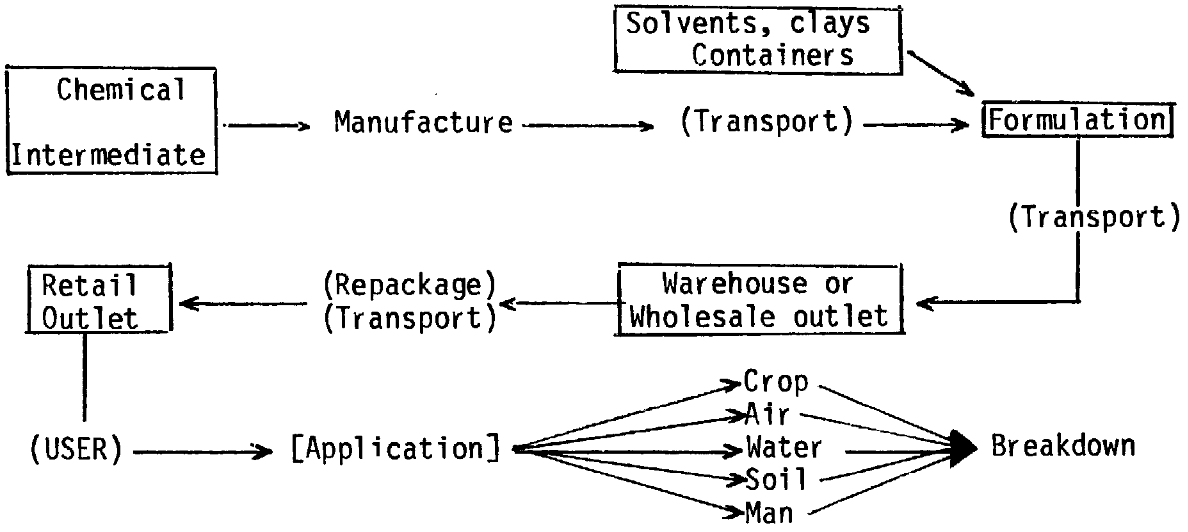
INTRODUCTION

Minimization of pollution in manufacture, formulation, transport, use, and disposal of pesticides can be achieved by a few common sense practices. These need not necessarily be costly, but do require prudent foresight and a reasonable attention to detail. In the manufacture, handling, use, and disposal of pesticides, it is impossible to prevent the escape of at least small amounts of the chemical. However, with the appropriate practices the amounts escaping need not be of such magnitude as to produce adverse effects. It is important for us to distinguish between the presence of trace level of contaminant that has little biological or environmental consequence as compared to amounts that we would call pollution in which observable effects may be noted. Thus, the mere presence of a chemical as detected by some highly sensitive analytical method is not necessarily cause for alarm. It should be kept in mind, as pointed out in a previous chapter, that it is the amount in the concentration, i.e., amount per unit weight or volume and the effects produced. This is the "dose/response" relationship so familiar to the toxicologist. Thus, at very low doses, i.e., slight contamination, there will probably be no observable effect.

The chemical flow

One may think of the various unit processes from manufacture to ultimate disposal of the chemical as a flow in which a chain of processes occur. The possibility of escape of the chemical exists at each step or link of the process, the intensity and amount will vary from step to step (Lawless et al., 1972). One must recognize that in fact the use of the chemical for pest control constitutes a purposeful release into the environment to accomplish beneficial and desirable ends (Green et al., 1977).

FLOW OF PESTICIDES THROUGH COMMERCE TO USE



The concentration in a nearby given volume of the environment or to which an organism is exposed will depend both on the amount released per unit (time) and whether it originates from a point source such as a manufacturing or formulating plant or an area source as when spraying a field. The highest concentrations are most likely to occur from effluent discharges, manufacture and formulating plants, the spills around warehouses, or in accidents during transport of technical and concentrated formulations. While substantial amounts of chemical may be applied to continuous areas in pest control operations, the amount per unit area (or concentration) will not be particularly high.

The object of adopting appropriate procedures to reduce pollution is to ensure that we do avoid the adverse effects on man and the environment. By observing the procedures, we can optimize the benefits to be derived from the use of such chemicals while minimizing the cost of the undesirable side effects (NAS/NRC, 1980). In the space available here, we can only hope to cover very briefly some of the procedures for reducing pollution at each step of the chain of processes from manufacture to use and disposal.

In manufacturing

Any manufacturing plant will require a reasonable technical staff of chemists and engineers who normally are quite conversant with means of reducing pollution from the manufacturing process (Lawless et al., 1972). Their job, of course, is made much easier if the plant is located well away from residential areas and away from streams and bodies of water that might become contaminated in the event of an accident or a spill. Manufacturing plants normally will have been engineered to provided for appropriate treatment of both the air and water effluent stream. These may be in the nature of a contract extractor to remove organics from water, treatment for gaseous or soluble effluents and appropriate filters for particulate matter (Pollution Control Technology, 1974). Likewise, the plant itself should be designed to have smooth, nonabsorbent floors (concrete) that can be washed down in the event of a spill. The drainage from such plants should go through a treatment process and a settling pond prior to discharge into sewers or streams. Other techniques for pollution reduction include either chemical treatment or incineration to destroy waste products and escapes (Kennedy et al., 1969). Likewise, such a manufacturing plant should have made provision for appropriate storage of containers of sturdy packages such as metal drums, plastic cans, or other types to prevent loss of the chemical (NAS/NRC, 1980; Pollution Control Technology, 1974).

In formulation and storage

It is inevitable that during handling and transfer of chemicals, that some will escape into the environment. In addition, there is always a problem of spills to be dealt with. Frequently, in transferring chemicals for formulation or during the formulation process itself, the chemical will volatilize into the air or some will be lost to the drainage system in the plant. Proper equipment for handling chemicals in formulation and packaging can go a long way towards reducing the pollution problems, but almost any plant needs some sort of pollution control devices for the small amount that will escape.

Before discussing some of the simple pollution control devices that might be used by a small plant, it is necessary to speak of the siting or location of such a plant and requirements for its construction. Such plants where at all possible, should be located away from areas of dense human activity and habitation. Another requirement is that they should be well removed from a location where surface runoff might carry chemicals into a waterway or sewer. When this is not possible, additional precautions are required to protect against pollution problems (Powers, 1976; Pollution Control Technology, 1974).

Formulating plants or repackaging and storage warehouses are likely to have fewer technical personnel with the knowledge of techniques and procedures for preventing or reducing pollution. It is important that these facilities be well designed in the beginning so that in the formulating of chemicals, repackaging, or storage, problems of pollution can be avoided. Again, with such installations location is extremely important. As indicated in a previous chapter, these should be located away from residential area, above flood zones and away from streams and bodies of water. Further, they should be properly equipped with supplies to deal with any spills or accidents that may occur.

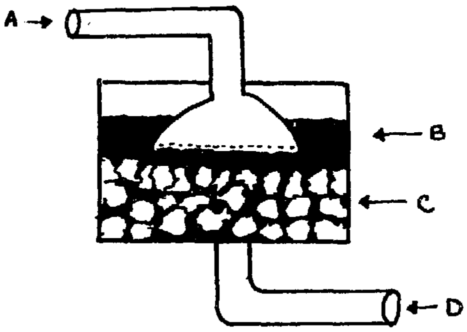
Any plant in which chemicals are made, formulated, or stored, should have concrete floors that are easily cleaned. Such floors could be sloped toward a drain that permits washing the floor down should a spill occur. The drain in this case should lead to some sort of lagoon or settling pond and not into the sewer. In fact, it is highly desirable in such a drain to have an appropriate treatment or adsorption filter to remove the chemical even before it goes into the settling pond or lagoon. In some cases a modest size trickling filter will be very useful (Pollution Control Technology, 1974).


Mixing chemicals

In formulating plants, air and water pollution involving both the parent chemical as well as solvents can be troublesome. However, with appropriate attention to adsorbent and particulate filters in the air flow system, settling ponds or adsorbent filters to deal with the water effluent, the pollution problem can be minimized. Many plants will utilize a hood with air flow system over the unit operations leading the air train into an appropriate type of filter often recovering a good deal of valuable chemical that can be returned to the formulating process (Pollution Control Technology, 1974). Some of these systems such as the carbon filter, the liquid extractor and particulate filters are illustrated with the drawings with this chapter.

Carbon filter for pollution prevention

As indicated above, pollution of air and water effluents coming from formulating plants are often a problem (Lawless et al., 1972). The carbon or charcoal filter mentioned for drains is quite effective in removing most organics from water. Such a filter is relatively inexpensive to construct and operate. Though activated charcoal may be the desirable material to use in such a filter, even crude grade of charcoal are quite effective and often are available locally. A filter two feet in diameter and ten feet long can often handle a million or more gallons of water before requiring replacement. The amount of water that can be filtered safely with such a drain will depend on the pollutant load.



Another technique that can be used in a formulating plant for removal of organic pesticides from the water is a contact extractor. This is a rather simple device where the contaminated water filters down through a layer of solvent as a fuel oil which extracts the organic. This is suitable for the oil soluble organics, but is not effective in the highly soluble forms. The water from this contact extractor is continually sipohoned out in order to keep the appropriate level.

As a final finishing step for a water effluent before it is discharged, is to hold it in a settling and degradation pond. Here, a residence time of a few days helps to further reduce the pollutant load.

Air pollution is another problem frequently encountered in formulating and storage plants. The pollution may be in the form of vapors of the chemical or it may be in dust. For worker safety, such plants should have a good forced air ventilation system. A single large fan properly ducted can remove dust and vapors from such a plant and from individual operations in the plant such as, filling bags, dissolving kettles, and solvent transfers.

Where solvent losses may be high, a condenser recovery system may prove to be valuable not only to reduce air pollution but also to recover the solvents. A simple water-cooled condenser in the airline often will be adequate for this purpose.

Where small amounts of vapors are the principal air contaminants, a charcoal filter in the ventilization system will often be quite effective. Usually, such charcoal filters will be fitted into the exhaust stack after the fan and become and integral part of the stack. A section in the exhaust stack two to three meters long fitted with an appropriate grade of sized charcoal is an effective aid in removing the vapors. It is necessary, of course, to replace the charcoal periodically so as to have a fresh adsorbing surface.

Where dusts are a problem (Lawless et al., 1972; Pollution Control Technology, 1974), a number of different types of dust traps are available. One of the simplest is the cyclone unit that is an integral part of the ducting system. Under proper operating conditions, the cyclone is quite effective and recovers a good deal of the material that would otherwise be lost. The bag house filter is another type of dust removal device. In this case, lage textile bags are connected to the ventilization system in an appropriate housing. One of the problems with the bag house filter, however is cost and the breakdown of the textile bag. A third type of device used for dust removal is a scrubber. In this instance, a large vessel is fitted into the ventilation system often in the stack and spray nozzles constantly wash the air stream. The water from such scrubbers, of course, must be filtered and cleaned up to avoid further pollution problems.

In major warehousing facilities, many of the same pollution abatement procedures as described above can be incorporated. In addition, however, because there will be many different containers to be handled and moved about, avoidance of pollution or at least its reduction, entails checking these containers to make sure of their integrity. Containers of chemicals should be handled with due recognition that they contain biologically active chemicals and therefore rough handling is to be avoided so as not to puncture or spill the chemical. Should the spill occur, however, the warehouse should be equipped with absorbent materials such as clay, charcoal, and lime to promptly treat the spill preventing its spreading and further escape. Perhaps as effective means of reducing the possibility of pollution as any is to assure that workers are properly trained in handling such materials and knowledgeable of the materials that they are dealing with.

In transport

Perhaps one of the most important precautions in avoiding pollution problems during transport is to ensure that the container is intact and in good condition so as not to rupture or spring a leak. Further, the container should be securely packed in the vehicle or the hold of the ship to avoid being broken loose and ruptured by contact with other containers, with something in the vehicle, or hauling of the carrier.

Should a container fall out of the carrier and spill on the roadway or along the side of the road, immediate steps should be taken to contain the spill so it does not spread. If nothing else is available as an absorbent, roadside soil shoveled onto the spill, if a liquid, will help to contain it. For a larger spill a small berm should be thrown up to prevent the spill from spreading. If at all possible, a trained crew should be called in to clean up the spill. (For materials to handle spills see chapter 15).

Selection of chemicals

The nature of the pest problem often determines the pesticide that must be used (Green et al., 1977). In other instances, there may be several pesticides that are equally effective each having a particular advantage or characteristic that should be considered. It is particularly important in choosing pesticides to consider how well that chemical fits into a good husbandry practice that is compatible with an integrated system of pest management. Thus, if a given chemical destroys a number of beneficial organisms while giving effective control of the pest, one might want to look for a chemical that could be used more selectively with less harm to the nontarget organisms (NAS/NRC, 1980).

The right chemical also calls for evaluation of its properties in relation to application. For example, if there were a choice between a volatile pesticide and one with less volatility, for the sake of protecting the operator, one would choose the less volatile. Similarly, if a chemical were applied to the soil, one of lower solubility and hence less likely to leach, would be chosen over an equally effective one that might tend to leach and thus cause water contamination.

Formulation of chemicals is also important. Unfortunately in the past, biologists paid little attention to adapting formulations to particular climatic and crop conditions, and the chemists were largely concerned with only seeing that the formulations had the appropriate shelf life and was convenient to use in the field. It has only been in recent years that attempts have been made to devise formulation to the chemicals that could withstand intense sunlight, resist wash-off by rain, and had less loss by volatility and hence, would be more effective and less likely to contribute to pollution.

In use

There are several instances during use and application where contamination with pesticides is likely to occur. This may begin with the place of storage or at the site of use where spills during transfer or a leaking container can result in contamination of the immediate area. For that reason, storage should be in a secure area well removed from other operations. Further, it should be situated such that there is not likely to be water pollution due to drainage from the area. An additional safety precaution is to attempt to assure that the storage area is not readily accessible to children or unauthorized individuals.

In the storage area, it is desirable to maintain a supply of an adsorbent material such as charcoal, vermiculite, or clays that can be used to help soak up any chemical spilled. Also, having a quantity of lime on hand would be desirable where organophosphates or carbamates are used. Sprinkling the area on which these chemicals are spilled with lime accelerates the breakdown and reduces the pollution hazard (Lawless et al., 1975).

Selection of chemicals

During application of a chemical, whether by air or ground, there is a possiblity of drift of a considerable amount of the material off the target area (Green et al., 1977). The amount of drift depends on the application equipment, how it is operated, the climatic condition, and the volume of carrier used during the application (see chapter 13).

Another factor, however, is drift that is enhanced by evaporation of the droplet. For example, if water is used as the carrier liquid in spraying, elevated temperature and low humidity results in rapid evaporation of the water reducing the size of the droplet. This results in additional drift of the spray material. For that reason, application during the cooler part of the day will result in less evaporation and reduce the tendency to drift. Also, wind conditions not only cause the droplets to drift but also increase rates of evaporation. To some extent, the rate of evaporation can be reduced through the use of appropriate additives, but not all additives are equally effective with all types of chemicals.

Once the chemical has reached the target area, it is distributed both on the plant surface and on the soil. Studies have shown that a substantial portion of the chemical applied to a row crop is deposited on the soil surface. Most of the chemical on the soil is quickly absorbed by the soil and held rather tenaciously. However, during the first few hours after application, particularly at elevated temperatures and in direct sunlight, some of the chemical will evaporate or volatilize off. There is little that can be done to control this short of tilling the chemical into the soil.

A significant contamination of water following application is by erosion of the soil to which the chemical is bound (McDowell et al., 1981). It has been shown in several studies that a good deal of the pesticides that get into water is carried there by the soil. As much as 0.1 - 5 percent of the chemical applied may reach bodies of water by erosion. The amount depends on the chemical soil type, slope, the time and intensity of the rainfall (McDowell et al., 1981; Wauchope & Leonard, 1980). This is also true in cities where runoff from lawns and streets will carry pesticides into the sewer and into streams. Erosion by either wind or water may carry the contaminated soil off the treated area.

A = road
H = house
R = river
C = crop growing in field
D = vegetative border
E = sump
F = field
B = field

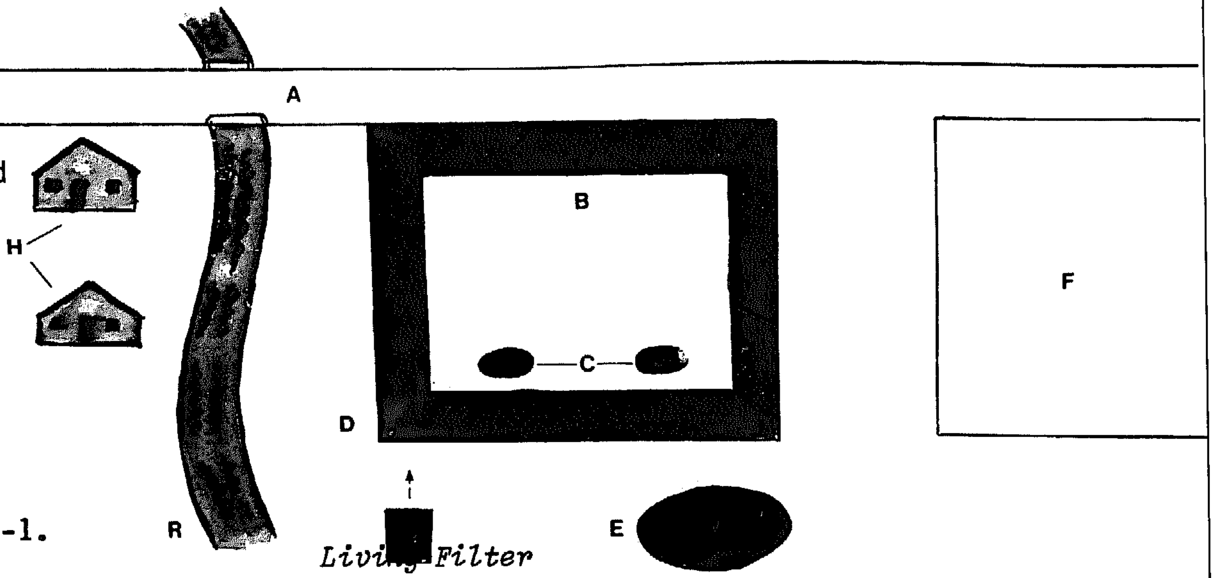


Figure 17-1.

Living Filter

There are techniques that can be used to prevent the contaminated soil being carried by runoff water into streams, irrigation ditches, or other bodies of water. These techniques are very simple, inexpensive and highly effective. Perhaps the simplest technique is to ensure that the treated fields have a border of vegetation around them, that is, having a strip of vegetation between the stream or body of water and the treated field (Figure 17-1.). Grass or broad-leaf plants are very effective in intercepting soil that is carried in surface drainage giving time for the chemical to break down. A narrow strip of grass, one to two meters wide, usually will

A = crop
B = field
C = sump
D = vegetative boundary
E = river

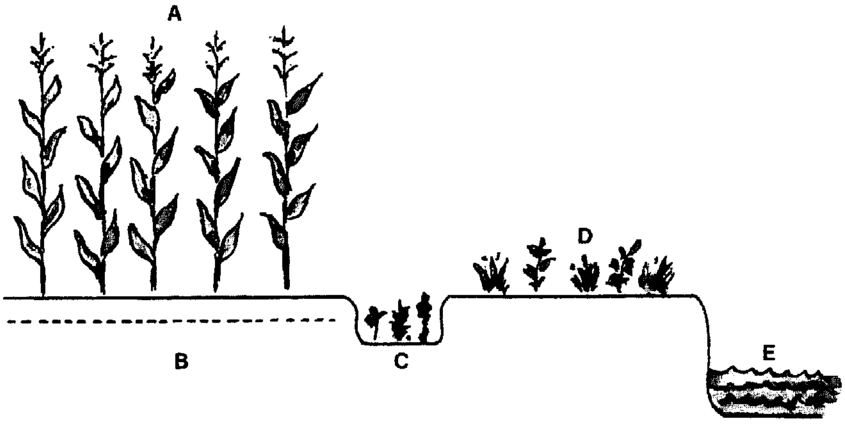


Figure 17-2.

Sump

be quite effective. Another simple technique is to grade the field and lead the drainage water from surface runoff into a depression or sump (Figure 17-2.). Such depressions or sumps a meter or two in diameter and something on the order of a quarter of a meter deep will handle the drainage from a rather large field. The sump is particularly effective it if also contains some standing vegetation, such as grass to intercept the water and filter out the soil that is carried.

Neither the sump nor the living filter represented by the border need take very much land out of production. Yet, such precautions can go a long way in preventing pollution through erosion by water.

In some areas, particularly with light soil, wind erosion can also carry contaminated soil off a treated field. Where the crop culture permits leaving vegetative residue on the surface of the soil, this can go a long way toward reducing wind erosion. Also a standing crop of almost any kind is highly effective.

In disposal

In the use and application of pesticides, one is confronted with the problem of disposal of excess or waste chemical and containers. Improper practices in disposal of chemicals and containers can result in pollution problems as well as a hazard to humans (Lawless et al., 1975). By following appropriate precautions and good practices in handling and disposal of pesticides and containers, these problems may be avoided (Lawless et al., 1972). For example, with containers used for liquids, much of the residual pesticide left in the container can be removed by immediately rinsing the container with a small amount of water or solvent and adding this to the spray tank. Rinsing a container at least three times with a small amount of water will reduce by upwards of 90 percent of the amount of chemical that would otherwise be left in the container (Lamberton et al., 1976). This practice has not only the advantage of reducing the possibility of pollution, but is good economy by using the last available amount of the chemical.

Having thoroughly rinsed the liquid container and added to the spray mixture, it is necessary to consider the method of disposal. One methods, of course, is to recycle the container to be used for the same pesticide. This is practicable for some, but not all containers. For those containers that must be discarded, safe burial is probably the most readily available for of disposal on the farm. Should this not be possible, then additional treatment of the container to remove as much of the residual chemical as possible should be practiced. Such treatment may include rinsing with a solvent such as oil and in the case of organophosphates or carbamates, treatment is to add water and a detergent together with some charcoal to remove additional quantities of the chemical. A word of warning is in order at this juncture. That is, that no pesticide container should ever be used for potable water or other foods for humans. (For further information on disposal see chapter 15.)

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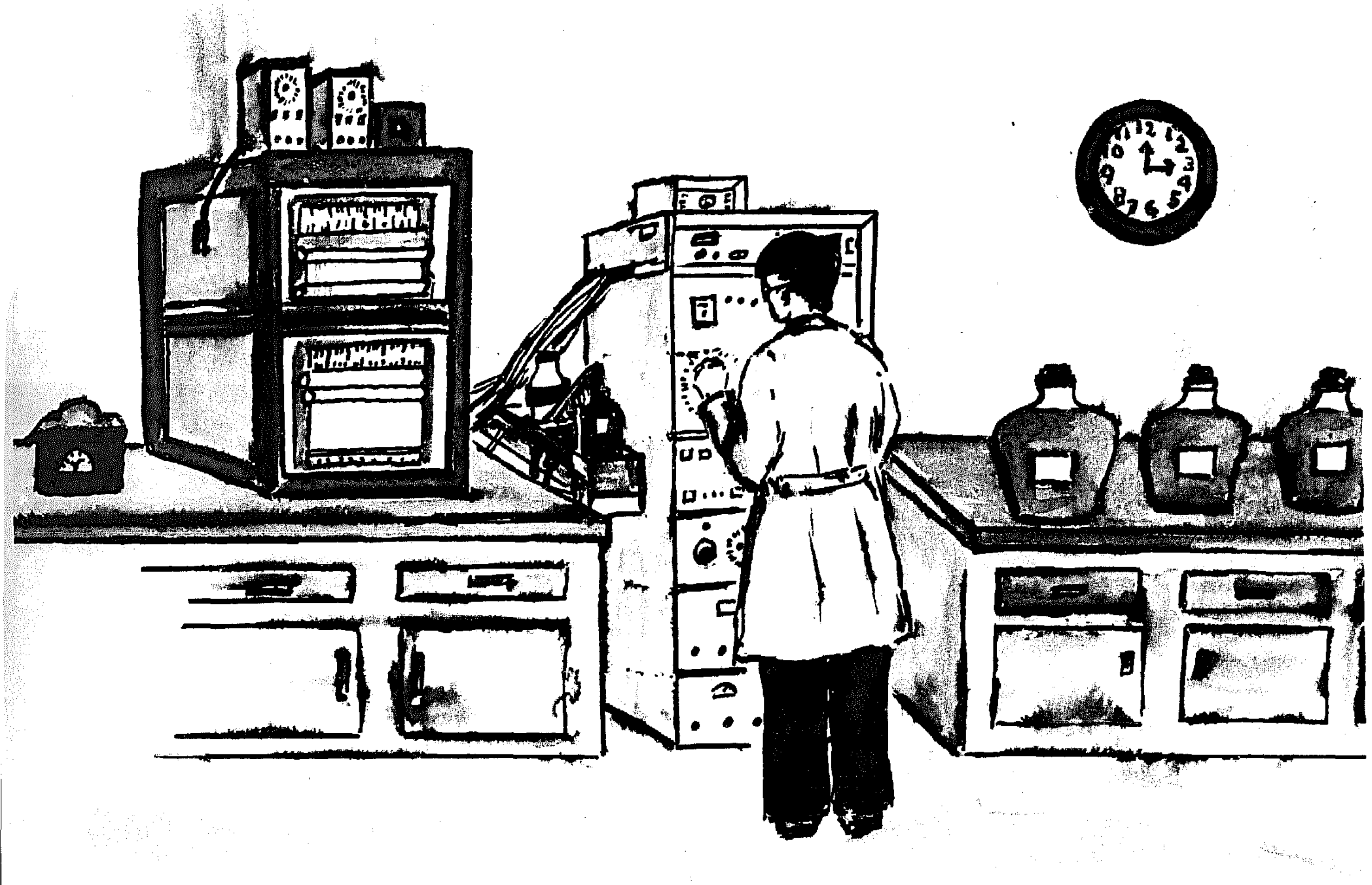
Chapter 18

The Role of the Laboratory in Pesticide Management

Freed, V.H. and Mann, J.B.



SUMMARY

The chemical laboratory plays a pivotal role in pesticide management. Without the ability to identify and measure the chemicals, it is difficult to formulate, assess residues, or monitor for contamination. The chemistry laboratory is capable of providing information on environmental behavior, persistence, hazards and residues. There are many methods of analyses, but the most commonly employed are thin-layer chromatography, gas chromatography and liquid chromatography. Thin-layer chromatography is cheap, rapid and easy to learn. It offers many advantages where resources are scarce and the ultimate in sensitivity are not required. A laboratory equipped with gas chromatography and other instruments can serve as a backup for many of the primary laboratories using simpler analyses.

INTRODUCTION

Pesticides are powerful and sophisticated technical tools. But these tools are not specific unless used in a knowledgeble and responsible manner. The harm they may cause can offset much of the good their use is intended to accomplish.

Studying Pesticides

It is often surprising to those not familiar with pesticide use and management to find the diversity of interests that are concerned with the use of these chemicals. Here we find the grower, chemical industry, physicians and public health officials, university people, ministries of agriculture and regulatory officials, and extension service all focusing their attention on pesticide management. It might be asked what prompts this concern? The answer, of course, stems from what was said earlier, that pesticides are powerful and sophisticated technical tools. They must be used responsibly to insure health and economic gains, prevent the development of untoward side effects such as resistance, avoid human poisoning, and protect the quality of the environment not only for this but succeeding generations.

There is a common core of knowledge that these diverse groups seek regarding pesticide management. Each wants to know which pesticide to use for a particular crop-pest problem, the cost of such use, the return to be expected, proper methods of use, and then the possibility of side effects such as residues, toxicity to man and other non-target organisms, and effects on environmental quality. In using pesticides, it is not enough to assume that we know the answers to these questions - it is vital that we do know. We may not have all of the answers to all of the question, but there is available to us a large body of information that can supply many of the answers. It is the responsibility of anyone having to do with the use of pesticides to devote time and energy to reading, asking questions, and applying common sense to gain the knowledge necessary for responsible use of the chemicals. Granted that the different agencies and individuals do not require the same knowledge to an equal degree since the information on given aspect of pesticide use depends on the particular role or responsibility. Nonetheless, a common core of knowledge and grasp of principles is a requisite to discharge the responsibilities and fulfill the appropriate role in pesticide management.

To illustrate some of the fundamentals that we should all be aware of in pesticide management, a few of the guidelines that might be considered are cited below:

1. Pesticides are essential for the control of many pests, but other methods of pest control are available such as cultivation, crop rotation, mixed cropping, biological control and ecosystem manipulation. We must be alert to use pesticides in such a manner as to be compatible with these other methods.

2. When pesticides are to be used, be sure that you know your chemical (properties, biological effects, methods of application, toxicity and persistence) and pest (life cycle, host plants, predators and population required for control).

3. Recognize that any chemical may be toxic to one or more organisms in sufficiently high doses but that the hazard from a chemical is not so much due to its intrinsic toxicity as the manner in which it is used. Therefore, in using a pesticide we should be guided as to time, place, and method of application, extent and frequency of application, by the hazards that might be entailed from the properties of the compound and the environment into which it is being introduced.

4. Both organisms and environment have a capacity for overcoming the effects of a reasonable amount of chemical. Therefore in the use of pesticides, every effort should be bent so as not to exceed the capacity of non-target organisms and the environment to deal with a particular chemical.

5. In the use of pesticides, carefully watch the application, the effects that follow, and where necessary take measurements (analyses) of residue levels.

6. Everyone associated with the management of pesticides should read, observe, ask questions and insist on answers.

These illustrate guidelines that those with a role and a responsibility in pesticide management can follow to obtain the knowledge necessary for proper use.

Because pesticides are chemicals, many of the important issues regarding their use depend on the chemistry of the materials. Therefore, chemical and biological laboratories have an important and even crucial role to play in pesticide management. It is from such laboratories that we obtain detailed information that will enable the industry, the applicator, the grower, the physician, and the regulatory official, to make wise decisions. To illustrate the important role of the laboratory, consider some of the questions for which we need answers in pesticide management and which we expect to be forthcoming from the laboratory:

1. What is the purity of quality of either a technical or formulated product?

Chemist at Work

2. If the chemical is formulated, how well is it formulated and is this formulation such that it will work under the particular conditions of anticipated application? How long is the product stable?

3. About the chemical itself, what are its properties? How long does it persist? Is it long enough to give adequate control? Does it persist so long as to become an environmental contaminant?

4. What residues may be encountered in food, feed, or the environment from the use of this particular pesticide?

5. What are the hazards to humans from this chemical?

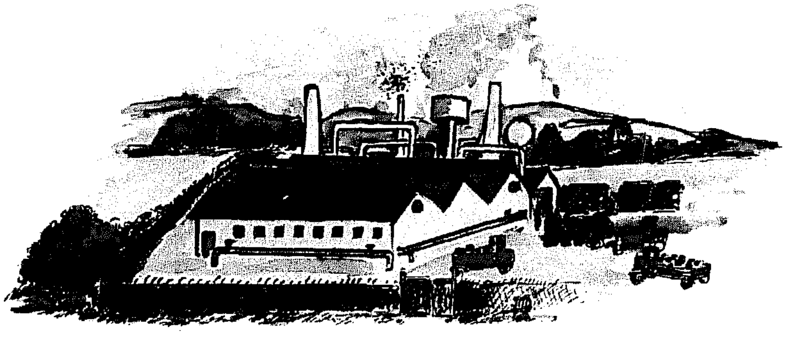
These and many other questions regarding the pesticide and its use can only be answered by careful laboratory work.

ROLES OF CHEMICAL LABORATORY

The laboratory, by careful and accurate work, can provide basic data on pesticides that is invaluable in pesticide management. In order to give a more precise understanding of the roles of the laboratory, let us attempt a brief description of some of the things that we can reasonably expect laboratories to do beginning with discovery and development of the chemical and carrying on through to its end use.

Discovery and Development

Practically every one of the pesticides that we use has been discovered and developed by the chemical industry. In order to find a compound suitable for insect, weed, or disease control, literally thousands of compounds will be prepared by the chemist and screened or tested for biological activity by the biologist. The discovery and development of a single effective and marketable pesticide by the chemical industry is a long and costly process. In the United States, it has been estimated that such a process may take 5 to 7 years and cost 8 to 10 million dollars before the



Manufacturing Pesticides

chemical is available for sale. During the development time, the laboratory is expected to provide detailed information on the chemical, its properties, method of preparation, and its important biological properties. A bit later in the process the laboratories should provide information on how to analyze for the chemical down to the residue level, how it will behave in the environment, methods of formulation, and finally, a good deal of information on its toxicology and metabolism.

By this time the chemical is probably going into field trials, and even into field use, but is improbable that the laboratory has provided all of the information that will be needed subsequently. Obtaining this information then, often becomes in part the responsibility of government and university laboratories. To see this, pick up the story of this particular pesticide as it enters into commerce.

Formulation Needed in The Use of the Chemical

The chemical company has now sold the material and it is being shipped for use in a tropical region. Before the chemical is paid for, we want to be sure that it is what is claimed to be and contains the right amount of the active ingredient. To ascertain this, a quality control analyses by the laboratory is needed. Beyond that however, it is desirable to be assured that the formulation purchased or to be made locally is suitable for the type of application intended. If it is an emulsifiable concentrate we need to check that it does emulsify properly in water, that the emulsion is stable, and that it wets the leaves or the soil as it should.

Analysis Needed for the Many Chemicals

It may be found in the laboratory that the compound meets the specified quality but in terms of its use under particular environmental conditions it is essential to ask whether or not the chemical has been properly formulated. This is a quite different question than asking whether the formula-emulsifies or suspends in water, or wets, and is sufficiently stable. Here, the question implies that the formulation should be designed to meet the particular environmental conditions of temperature, sunlight, rainfall, and the croping conditions so as to give the safest and most effective pest control for the least amount of money. But in addition to this, we want a formulation with a minimum amount of drift and evaporative loss. Part of this information will come from studies on environmental behavior and fate of the chemical, or chemodynamics. The measured physical properties and behavior can be used as a guide in the formulation.

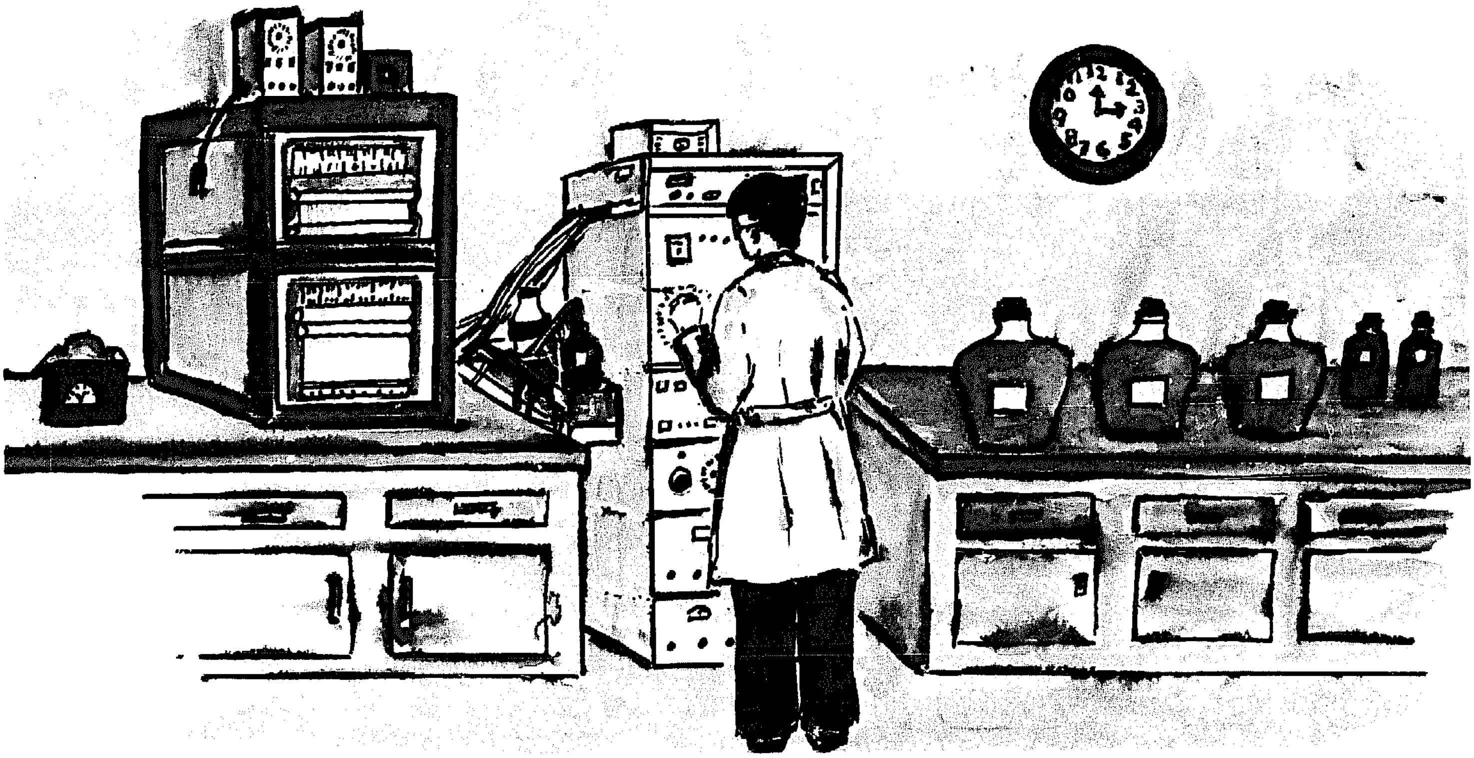
Environmental Behavior and Fate

To make effective and safe use of pesticides, it is necessary to know something of how they behave in the environment--such as the amount that evaporates, how readily do they leach in soil, how rapidly do they breakdown, how far do they transport, and do they accumulate in other organisms? Much of this can be learned by observations and measurements in the field, but this requires a considerable period of time before the information is gathered. It is possible by appropriate measurements in the laboratory to get basic information that allows predictions to be made about the behavior of a chemical when in wide scale use. To be sure, this laboratory work needs to be validated by the field observations and measurements, but the basic work tells us what questions to ask and where to look for answers. It should be added also, that this type of study is not expensive in terms of either manpower or time and hence can be provided readily by many of the laboratories now in operation.

Handling and Disposal

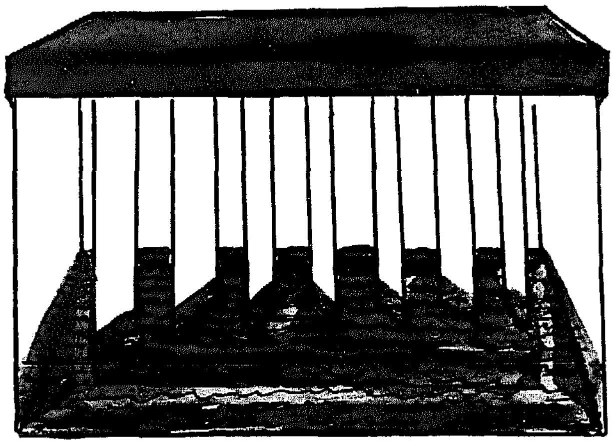
An inevitable problem when using large amounts of chemicals, as is the case with pesticides, is that of disposing of leftover quantities, stocks that have deteriorated, breakdown and by-products, and of course the containers used. Here again, the laboratory has a role in providing information that will serve as a guideline for disposal of the chemical. For example, the laboratory can tell us whether the chemical is sufficiently reactive with another chemical. Laboratory studies can also tell us whether the chemical is water soluble and not sufficiently adsorptive on soil to permit its disposal in soil, particularly near water supplies. Knowing the chemistry of the compound can also give valuable information on how to clean and dispose of containers which may be used for the chemical. Again, this is not a difficult nor demanding role for the laboratory if the laboratory is doing the right kind of studies.

Analyses--Clinical and Residue



Anaylsis by Gas Chromatography

One of the most important roles that a laboratory plays in pesticide management is providing accurate and reliable analyses for pesticides. Analyses may be made to determine residues in food or feed, or it may be the identification and quantitation of a pesticide involved in human poisoning. Actually, analyses are fundamental to all the other roles described for the laboratory. Without a method of analyses, or if the method is unreliable the other information has little meaning. It is important therefore that the laboratory having responsibility for analyses know precisely what it is analyzing for, how to perform this analysis, how to check to make sure the analyses are accurate, the level of sensitivity that is needed for a particular problem, and which methods, if several are available, should be used.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Simple Equipment Needed
for Thin-layer Chromatography

Most are familiar with the fact that there are a variety of different analytical methods. They range from biological assay to spectrophotometry to various types of chromatography such as gas chromatography, liquid chromatography, thin-layer chromatography, to the combination of gas chromatographs and mass spectrometers coupled with computers. Each method has its advantages and disadvantages in terms of time required, sensitivity, accuracy, and reliability. It is important that an analytical laboratory be familiar with all these methods, their advantages and disadvantages, and select the one that is suited to the problem. For example, in quality control work the use of the most sensitive of gas chromatographic techniques may lead to errors in the analyses. The reason for this is that the method is so sensitive to small amounts of chemical that great dilutions must be made in order to get the chemical in a low enough concentration to inject into the gas chromatograph. There is a likelihood of error creeping into the dilution process that then gives erroneous results. It would be far better to use a spectrophotometric method such as infrared spectrophotometry which can be applied directly. On the other hand, if one wanted to measure a material down to a tenth of a part per million, spectrophotometry or thin-layer chromatography may be too insensitive.

Very often a less sensitive but more convenient (and less expensive) method will satisfy the needs. This is a special consideration where maintenance or service of sophisticated instruments may be a problem.

Another responsibility that the analytical laboratory has in analyses is to make sure that everything is operating properly so as to give the right answers. For example, in gas chromatography, there are not only many opportunities for mistakes in extraction and purification, but for one reason or another the instrument may not be performing properly. In addition, if the wrong column is being used, or the column is dirty, or the detector is malfunctioning, or there something in the sample that masks the residue, this could result in wrong answers. The analyst therefore must take special precautions to avoid these problems.

One of the means by which these inaccuracies are to be avoided is to use good analytical standards of the chemical being determined. By carrying the sample through with a standard, one has a check on the analytical method. Even better--if there is more than one analyst in the laboratory--is to have an intralaboratory quality assurance program where not only the sample but also certified control samples are analyzed by more than one chemist and the results compared. Even greater reliability can be achieved when different instruments can be used for the same measurement.

In addition to checking the accuracy of the method, it is highly important the laboratory have suitable checks to make sure that what is being measured is really the chemical being sought. This can be done only through proper confirmatory tests. All too often it is assumed that using some variation of the same method of analyses, such as two different columns and detectors in gas chromatography, is adequate for confirmation. This is not the case. Where confirmatory analyses is required, two distinctly different methods of analyses should be attempted; for example, mass spectrometry and gas chromatography.

A laboratory having capability for gas chromatography and other methods of analyses requiring sophisticated instruments is expensive. Resources do not always permit developing such laboratories, however desirable it may be. However, quite good analytical work can be done with much simpler and easily maintained equipment. Advances in thin-layer chromatography now allow quite good sensitivity in both quantitative and qualitative analyses of many pesticides. The technique is easily learned, the equipment simple and inexpensive, and the method reasonably rapid. Where cost is a factor or equipment, supplies and maintenance difficulty, thin-layer chromatography offers an attractive alternative for pesticide analyses.

Finally, one other highly recommended aspect of the analytical laboratory practice should be mentioned; that is the interlaboratory quality assurance program. In this program one laboratory undertakes to provide:

a. reference analytical standards, and

b. spiked samples to all the other laboratories for analyses.

After each laboratory has run the analyses and reported the results back to the referee laboratory, these results are analyzed and compared. From this exercise a great deal may be learned about the difficulties a particular laboratory is experiencing in analytical procedure. Often, one can detect difficulties in extraction and purification, in operation of of the instruments, or contamination of solvents. The quality assurance program is handled in such a way as not to embarrass any laboratory for, after all, any chemist can make a mistake. The quality assurance program is intended to be a means by which various laboratories can help one another to maintain the best order of accuracy and reliability that is possible to achieve. It is a program of great benefit not only to the laboratories but to all that they serve.

The following tabulation gives the order of sensitivity for some of the available analytical methods:

APPROXIMATE SENSITIVITIES OF SOME ANALYTICAL METHODS FOR PESTICIDES

Methods of Analyses	Sensitivity [1]
1. Bioassay	0.5 µg
2. Spectrophotometry	
Ultraviolet	0.1 µg
Infrared	0.5 µg
Fluorescence	1.0 µg
NMR	1.0 mg
3. Colorimetry	5-10 µg
4. Chromatography	
Paper	1-10 µg
Thin layer	0.01-1.0 µg
Liquid	0.5-1.0 ng
GLC (detector)	
Flame	1.0 ng
Flame Photometric	0.01-1.0 ng
Microcouleometric	0.1 ng
Conductivity	0.3 ng
Electron Capture	1.0 Pg
Mass Spectrometer	1.0 µg
5. Polargraphy	0.5 µg

[1] 1mg = 10^{-3}g, 1 µg = 10^{-6}g, 1 ng = 10^{-9}g, 1Pg = 10^{-12}g

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Chapter 19

Nutrition and Pesticide Interactions

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Freed, V.H. and Davies, J.E.

SUMMARY

In the fields of nutrition and agromedicine have an exciting research, service and training future together. The specific subject of nutritional status and pesticide toxicity is only one research area that demonstrates how fruitful this new partnership can be. Its synergism can do much to assist the social, health and nutritional status of our fellow humans in many parts of the world.

INTRODUCTION

The interaction of nutritional factors with pesticide toxicity is a relatively new and exciting concept. As malnutrition continues to remain the major international health problem, and as pesticide usage increases, the interaction between malnutrition and pesticide toxicity will merit increasing research and public health. Indeed, the role of pesticides in health is like a two-edged sword. They can be used with skill to increase crop yields and help prevent malnutrition; or they may be used carelessly to induce illness and death by adding the insult of pesticide toxicity to the injury of malnutrition. The purpose of this chapter is to consider how pesticides and nutrition interact, and to illustrate these interfaces with specific examples rather than present a complete review of the literature.

How may pesticides influence dietary and nutritional status? Pesticides may 1) decrease appetite and induce weight loss; 2) alter nutrient requirements; 3) affect micro and macronutrient storage sites (ex. liver); 4) affect specific metabolic pathways; 5) increase excretion of nutrients or their metabolites; 6) compete for a specific blood-binding site of a micronutrient, viz. a pesticide may require a protein fraction such as albumin as a carrier and displace vitamin A; 7) bind with a moiety of nutritional significance, viz. dieldrin binds with hemoglobin and albumin; 8) trigger a metabolic effect which increases the risk of disease, viz. DDT induces hyperlipoproteinemia, as it is transported in low density lipoproteins; 9) may injure the microsomal fractions necessary for enzyme induction, which in turn are required for metabolic and detoxifying processes; and 10) be distributed in organ systems which have nutrient digestive, utilization, absorption and excretion functions, ex. dieldrin is excreted into bile and pancreatic juice, which may then influence dietary nutrient absorptions.

To consider the converse question, how may nutritional status influence pesticide toxicity? Pesticides may 1) be more soluble in specific dietary components, ex. lipids; 2) concentrate more or less of a given pesticide residue in obese individuals; 3) have predilection for persons on specific diet patterns, viz. Indian vegetarians have higher DDT residues than nonvegetarians; 4) increase or decrease in concentration of certain tissues as a result of weight loss (ex. liver); and 5) increase in toxicity if an individual, particularly a farm worker, is either generally malnourished or has a specific micronutrient deficiency.

Protein

In 1969, Boyd and his colleagues studied the effect of a wide range of protein intakes on the toxicity of many pesticides in the rat (Boyd and Dobbs, 1969). Shakman analyzed these experiments and concluded that at:

1. one-third normal dietary protein, toxicity for any pesticide is minimally increased,
2. one-seventh normal protein intake, carbaryl, parathion and captan are markedly increased in toxicity, and
3. at less than one-seventh normal intake of protein, the toxicity of heptachlor and dimethoate is unchanged. (Shakman, 1974).

Boyd and Chen (1968) used a specific dietary regimen to induce growth stunting, and reported that rats given this regimen were twice as susceptible to the toxic effects of lindane as the controls fed a normal rat diet. Boyd further indicates that the type, as well as the amount of protein influences pesticide toxicity since lab chow, which contains predominantly plant proteins, appears to increase the toxicity of endrin, while decreas- that of CIPC. In Boyd's experiments, the dietary protein manipulated was casein. However, the total dietary intake given the experimental animal must be carefully considered. The growth and development of the rat is sensitive to a wide range of macro and micronutrients which are capable of influencing the growth and metabolic integrity of many organ systems. Moreover nutrients interact in such numerous and complex ways that they further influence a wide range of substrates and enzyme systems. Boyd et al. (1968) also induced a kwashiokor-like state in rats on a protein deficient diet, and studied the toxic effects of carbaryl, which was found to be more toxic in protein deficient rats.

By contrast, decreased intake of dietary protein may also decrease the toxicity of a pesticide. Weatherholtz, Campbell and Webb (1968) studied the effect of 5, 20 and 40% casein diets on heptachlor toxicity. Rats fed 20 and 40% protein diets produced more of the toxic metabolite heptachlor epoxide, compared to those fed a 5% casein diet. These authors speculate that populations on low protein diets who are exposed to heptachlor, and possibly other enzymatically activated toxicants, may be less affected than well-fed populations. Heptachlor is in fact used frequently in developing countries.

In addition to studies on the type and amount of dietary protein, investigators have recently turned to a study of how pesticides may influence the metabolism of specific amino acids. Mehrle and DeClue (1972) studied the chronic effect of dietary dieldrin on phenylalanine and its metabolism in the rainbow trout. Dieldrin is one of the most prevalent pesticides in our aquatic environment; it is found in 93% of fish samples across the United States in quantities of 0.01 - 1.6 ppm. Dieldrin increases urinary phenylalanine by 50% in the trout and alters the concentrations of 10 other amino acids. In addition, brain enzymes such as glutamine transferase, glutamate dehydrogenase, glutamate-pyruvate transaminase and glutamate-oxaloacetate transaminase are affected, as well as the concentration of nine amino acids in the brain. Dieldrin also was found to decrease liver phenylalanine hydroxylase and increase serum phenylalanine concentration. Mehrle and DeClue have also found that chronic dieldrin intake may decrease phenylalanine hydroxylase activity of the rat. If similar observations are ever made in man, one can only wonder whether phenylketonuria might ever be induced by pesticides like dieldrin. Indeed fascinating studies by Tocci, et al. (1969), have clearly shown that persons occupationally exposed to pesticides have altered plasma amino acid concentrations.

Turning to another amino acid, Tinsley and Claeys studied the influence of dietary methionine on DDT metabolism in the rat and observed an increase of DDT and DDE in liver with increasing intake of methionine (1970).

An illustration of how nutritional states may influence pesticide toxicity is the investigation of Lee, et al. (1968), who gave rats a high protein (25%) diet, which afforded protection against dieldrin toxicity. On the other hand, Boyd and De Costra (1968) showed that rats given high protein diets exhibit increased urinary and fecal excretion of DDT metabolites.

Fats

Organochlorine pesticides are of course soluble in the adipose tissue of many species including man. Weight loss can induce mobilization of fat soluble pesticides such as DDT and result in elevated blood levels which are toxic to the central nervous system. By contrast, Keane et al. (1969), were able to alleviate toxic symptoms in dieldrin-poisoned dogs by force feeding them high calorie diets. Obese mammals, fish and birds are apparently more resistant to DDT toxicity than their controls. However, with the mass preoccupation of weight loss in Western countries, one can only wonder whether metabolic hazards may be induced by pesticides periodically leaked into the circulation during weight reduction (Davison, et al., 1970).

While Durham (1967) reports that the quantity of dietary cholesterol and the degree of saturation of dietary lipids does not affect DDT toxicity, dieldrin appears to interact with unsaturated fatty acids and potentiates essential fatty acid deficiency. This effect is apparently enhanced by both riboflavin and nicotinic acid-deficiency. These observations also have considerable implications for malnourished populations.

The work of Nedkova-Bratanova (Tinsley, 1968) illustrates how certain pesticides may influence macronutrient absorption via decreasing intestinal enzymes. They showed that phosalone and lindane given to rats markedly decreased the activity of intestinal mucosal disaccharidases, especially surcrase, while slightly to moderately decreasing such jejunal and ileal dipeptidases as glycyl-L-leucine, glycyl-L-valine and L-alanyl-glycine dipeptidases.

Work in rats that could have importance to the populations of developing nations is that of Dale (1975), who showed that starved rats mobilized DDT from adipose tissue and thereby increased plasma, kidney and liver concentration.

Vitamins

Vitamin C

Vitamins as well as proteins and lipids play important roles in modifying pesticide toxicity. Wagstaff et al. (1971) induced ascorbic acid deficiency in guinea pigs and noted reduced induction of microsomal enzymes by dieldrin. In addition to its known functions in preserving capillary integrity, more recent evidence indicates that ascorbic acid may partially control oxido-reduction states of living cells. Moreover, vitamin C has been shown to play an important role in various drug metabolizing enzymes in guinea pigs. Perhaps even more significantly, agents which induce drug metabolizing enzymes stimulate the excretion of L-asorbic acid through the glucuronic acid pathway. Ascorbic acid deficiency also significantly impairs o-methylene induction and the stimulation of the glucuronic acid system by DDT (Chadwick et al., 1971). Thus the vitamin C status of a given population group may determine, at least in part, its response to DDT and

DDT-like pesticide exposure, and may thus influence the risk of pesticide toxicity. Wagstaff and Street (1971) demonstrated decreased enzymatic induction (o-demethylase and aniline oxidase) by 25 ppm dieldrin in ascorbic acid deficient guinea pigs.

Vitamin A

The effect of pesticides on liver storage of vitamin A has merited considerable attention. DDT and dieldrin reduce liver content of vitamin A, and it has been hypothesized that vitamin A deficiency may increase the toxicity of pesticides. Philips, as early as 1962, fed rats from 0 to 100 ppm of DDT and studied the utilization of orally administered carotene. The feeding of more than 10 ppm DDT decreased liver stores of vitamin A. Phillips and Yidiroglou (1965) conducted field studies which revealed that liver stores of vitamin A were decreased in yearling beef steers fed with forage sprayed with DDT. An interaction between type of dietary protein and vitamin A is illustrated by the work of Tinsley. Rats fed soybean protein and exposed to DDT exhibit depressed growth and decreased liver vitamin A. Soybeans are deficient in methionine, and when this amino acid is added to the diet, the effects of DDT are reversed.

How pesticides may alter nutrient requirements may be exemplified by the work of Sikes-Bridges (1952) who were able to produce experimental hyperkeratosis by administering chlorinated naphthalene compounds, which influenced Vitamin A metabolism. Phillips (1965) further demonstrated decreased utilization of carotene and Vitamin A and decreased liver stores of Vitamin A by feeding rats 10 ppm DDT for 72 days. Tinsley (1969) reported that DDT-induced decreased liver stores of Vitamin A was inversely related to dietary methionine, and in 1976, Davison also found that methoxychlor at concentrations of 1000 ppm or higher liver stores of Vitamin A in rats was reduced.

Vitamin D

The chlorinated hydrocarbon insecticides such as DDT and its principal metabolite DDE interfere with calcium metabolism of various avian species (Novicki, et al., 1972; Edwards, 1970; Hickey and Anderson, 1968; Ratcliffe, 1967), thus affecting the reproduction process by decreasing the egg shell weight and thickness (Hickey and Anderson, 1968). This process appears to be mediated by disrupting the normal function of vitamin D: DDT isomers, o,p'-DDT or p,p'-DDT, treatment reduced vitamin-D_3-mediated intestinal calcium absorption (Novicki, et al., 1972a). However, the mechanism of how the organochlorine insecticides modify the vitamin D and calcium metabolism remains to be established, since neither the levels of 25-hy-droxycholecalcifecol; nor 1,25-dihydroxcyholecalcifecol are affected by DDT treatment (Novicki, et al., 1972a; Kenny 1974).

Vitamin B

In an effort to study the interaction of dieldrin with thiamin, Tinsley (1968) placed rats on a thiamin deficient diet and subjected them to rations containing 20 and 200 ppm dieldrin. Growth curves of the rats suggested that dieldrin afforded some protection against thiamin deficiency.

The effect of marginal riboflavin deficiency on dieldrin toxicity was studied by Tinsley (1966). Enhanced dieldrin toxicity was noted in the riboflavin deficient rats given 20-30 ppm dieldrin, including higher liver residues.

Vitamin E

Hunt and McCarty (1972) found that decreases in serum Vitamin E, carotene and fatty acid levels occurred in calves exposed to moderate organophosphate insecticides in humans. Bus, et al. (1976), studied Vitamin E and selenium deficient mice and found they had enhanced susceptibility to paraquat tox- icity. Moreover, dietary supplementation by Vitamin E and selenium provided protection against paraquat toxicity (Bus, et al., 1975). Welsh (1976) found that Vitamin E was effective in protecting the rat against methyl mercury toxicity; selenium also exhibits protective effects on the toxicity of this agent.

Malnutrition, Pesticides and Behavior

It is with both caution and fascination that a new area of research can now be approached: the relationship of pesticide intake and dietary pattern to behavioral changes. Casterline, Brodie and Sobotka (1971) explored the effect of banol and parathion on operant learning behavior of rats fed adequate and inadequate casein diets. Markedly detrimental effects on rat operant performance, i.e. lever press to prevent electric shock, was observed in protein deficient rats given banol and parathion. The combination of low protein diet and these pesticides apparently synergistically affected operant behavior. The reported retarded behavioral performance was not accompanied by changes in cerebral or cerebellar cholinesterase or monamine oxidase concentrations. However, other studies have shown that brain cholinesterase activity is inhibited by parathion and banol in rats fed an 8% casein diet. It is conjectured that early brain enzyme changes may induce conditioning effects which persist after the brain enzyme levels return to normal. The potential significance of the findings of Casterline and his collegues are enormous. It has been shown that diet can influence neurotransmitter concentration and functioning in the brain. Recently we have attempted to formulate a "field theory" which relates chronic suboptimal nutritional status in children to potential effects in cerebral histochemical development and neurotransmitter functions, which in turn may contribute to socially deviant behavioral patterns in children (Christakis, et al., Monograph prepared for publication).

PESTICIDES AND THE PATHOLOGY OF MALNUTRITION

Pesticides enter the body through the skin, respiratory system and the gastrointestinal tract, the latter as a result of contaminated food or suicidal or homicidal intent. Considering skin first, it is of interest that many nutrients affect the integrity of this most important barrier to infection and injury. Vitamin A is responsible for normal skin epithelium in conjunctivae. Ascorbic acid maintains the intracellular cement substance of the skin and its delicate vascular system. Protein, niacin and linoleic acid deficiency can cause skin lesions such as thickening and cracking of the skin, severe dermatitis, and hyperpigmentation. This may also affect the absorption of pesticides through the skin.

A number of B vitamins affect the skin of the eyes, nose, lips, tongue and the borders between the skin and mucous membranes of the mouth. Thus riboflavin deficiency causes swelling and fissures of the inner corners of the eyes and mouth; pyridoxal phosphate or B_6 deficiency induces nasolabial dyssebacia. Several vitamin deficiencies can cause lesions of the tongue by making its surface smooth through atrophy of the filiform and fungiform papillae, such as folic acid, iron, B_6 and riboflavin.

All of the above lesions afford an opportunity for pesticides to enter the skin or mucous membranes and the blood stream more quickly, and potentially enhance their toxicity. For the farmer or pesticide technician, the major portal of entry is the skin. Optimal nutritional status is mandatory to avoid the potentially increased absorption which may occur through dermatologic nutritional pathology.

The respiratory tract is also a portal of entry for pesticides, especially for the families of farm workers living near fields which are aerially sprayed with pesticides. Smoking and nutritional factors can influence the integrity of the respiratory epithelium appreciably. Smoking causes paralysis of the celia of the epithelium of the respiratory tract. Thus particles, are retained rather than driven up the respiratory tract where they can be expectorated.

Vitamin A is very necessary to the maintenance of normal respiratory epithelium and its vital physiologic roles. Inadequate vitamin A may make the cells lining the respiratory tract more permeable to pesticides. There are data to suggest that workers with low vitamin A levels exposed to carcinogenic industrial environmental pollutants are more susceptible to lung cancer than workers with normal vitamin A levels (Fraumeni, 1975).

The third portal of entry of pesticides, particularly for the public, is chronic low level ingestion through food entering the gastrointestinal tract. Here an interesting series of research questions can be proposed. What is the solubility and gastrointestinal absorption characteristics of pesticides consumed in association with various diets? Do high fat diets increase the absorption of pesticides? Does severe malnutrition change the ability of the GI tract to absorb nutrients or pesticides? Does a high fiber diet sequester or chelate pesticides and thus perhaps partially prevent the absorption of pesticides?

Indeed acute or chronic protein calorie malnutrition, or acute or chronic bacterial, viral or parasitic infections may affect the normal histology of the gastrointestinal tract of both children and adults. The normal convolutions of the gastrointestinal tract are lost as the multiple folds and rugae are sloughed off together with the delicate brush border of the cells which regulates nutrient absorption. This may have a profound effect on the absorption characteristics of the pesticide resulting in uninhibited and/or unconjugated absorption directly into the vascular or lymph system. The disuse atrophy of the gastrointestinal tract epithelium in patients who are chronically malnourished due to a host of diseases -- both physical and psychosocial -- may also contribute to pesticide toxicity.

We may conjecture that high fiber diets may decrease the absorption of pesticides in the same way as it decreases the absorption of cholesterol, zinc and iron; it is not unreasonable to hypothesize that it may physicochemically combine with pesticides. In this regard, the diets of Mediterranean and Latin American nations are much more adeuqate in food fiber compared to the relatively refined low fiber diets of North America and Europe. Thus ethnic diet patterns may influence pesticide toxicity.

Calabrese (1980) has done public health a service by documenting in detail the influence of nutritional status on pollutant toxicity, including pesticides. Moreover he has had the courage to consider the difficult and politically abrasive questions regarding:

1. the adequacy of RDA for those specific micronutrients which appear to have a role in decreasing the toxic effects of pesticides, or when inadequate ingested may enhance toxicity;

2. whether marginal vitamin deficiencies may enhance pesticide toxicity;

3. whether the RDA for amino acids are capable of assuring maximum enzyme inductive rates with respect to DDT-lindane;

4. chronic low-level organic and organophosphate insecticides may affect vitamin E status in humans.

From the above considerations, it is obvious that two key environmental variables - the dietary and nutritional status of the organism, and pesticides - interact in ways which can serve to protect against, or enhance, their metabolic effects. The implications for human populations are both real and enormous. From the viewpoint of nutrition, the current RDA's may prove inadequate if specific micronutrients such as Vitamins A, C and E are definitely shown to protect against environmental toxicants. Moreover body composition, i.e., relative amount of lean muscle mass and perhaps its specific proportion of individual fatty acids may influence the nutrition-pesticide interaction.

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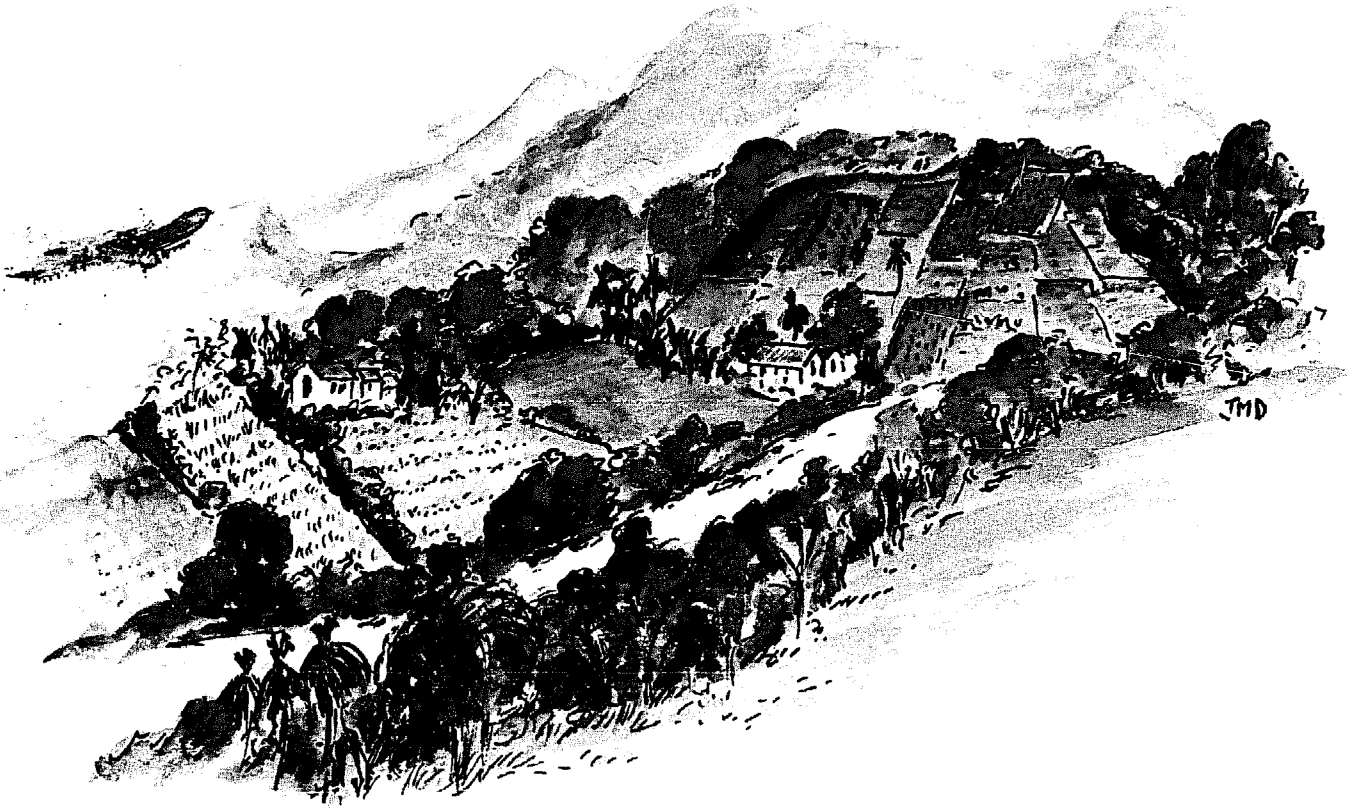
Chapter 20

Regional Differences of Agromedical Problems



SUMMARY

This chapter outlines features of the tropical region as they relate to pesticide protection. Three major areas are examined: public health diseases, geographical factors influencing chemical persistence and geographical impacts on agromedicine. The need is emphasized for tropical countries to develop relevant intermediate technology and an infrastructure which would allow the increasing quantities of pesticides in the region to be used with maximum human and environmental safety.

The implications of this increased use of pesticides in the tropics are discussed in this chapter. Reference will be made to the actual or potential effects of pesticide use on human and environmental health in the area. Focus will be directed on possible solutions for problems which have been identified.

I. Agromedical Problems in Humid Tropical Areas

by Janice Reid

Previous chapters have dealt with general principles of efficient pesticide management and the guidelines for implementation of these principles to reduce the levels of human exposure to pesticides. However, some of these assume different significance in the humid tropics.

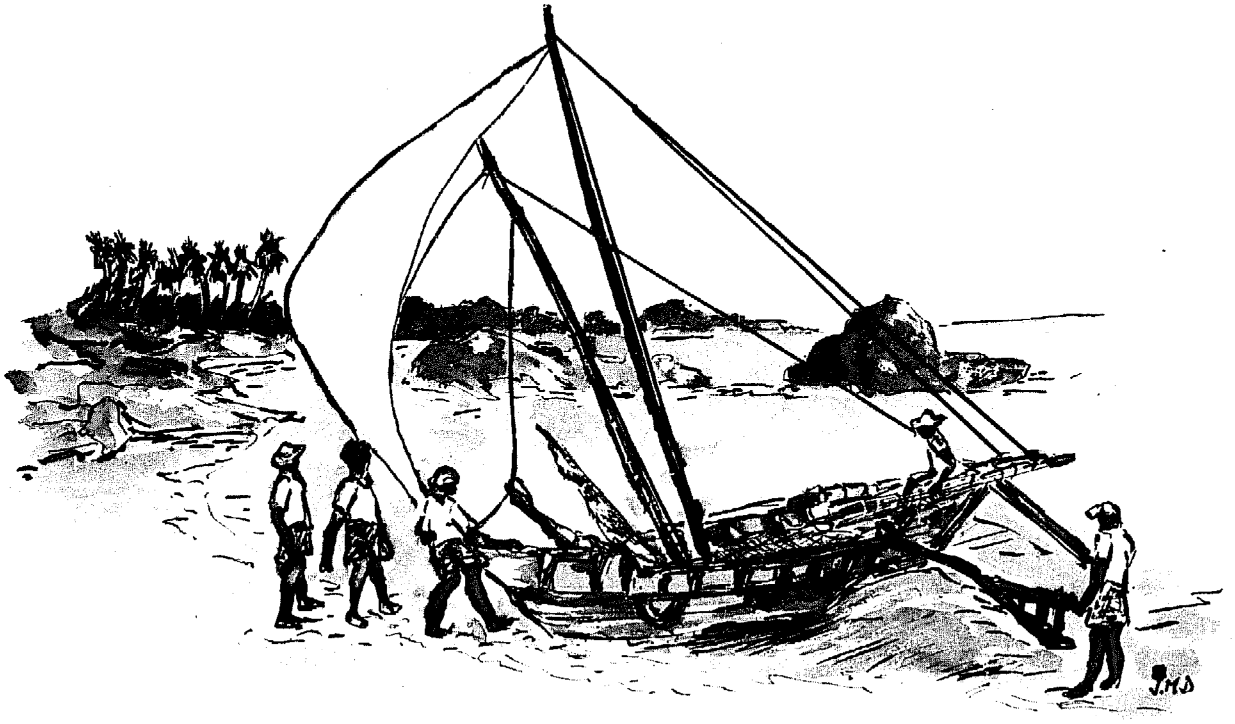
At the outset for the sake of clarification, we should define the special geographical areas we will be discussing here. It will denote all those areas of the tropics between latitudes 23° North and South where annual rainfall exceeds annual evapotranspiration loss. In some areas, this condition may be experienced for only part of the year e.g. in the semi-arid areas of the Caribbean, Africa and the East.

The climate of countries in the humid tropics fosters multiplication of ectoparasites and vectors of human and animal diseases e.g. malaria, bilharzia, yellow fever, dengue onchocerciasis and equine encephalitis. From 50 - 90% of the economy of these areas is based on agriculture - much of which has historically been directed towards the production of export crops on a plantation type system. Support labor is derived largely from semi-skilled peasant families who are also responsible for producing much of the food for local consumption. The recent world food crisis has placed increasing stress on the need for tropical countries to produce more food for export and local consumption.

In both urban and health areas as well as in agriculture, pesticides are relied upon as a quick way to reduce the ravages from pests and diseases. This is reflected in the rapid increase in the quantity of pesticides being imported and sometimes manufactured in tropical countries. Since the mid 1960s, the quantity of pesticides used in Africa has increased fivefold (Cultural Survival, 1981), has quadrupled in Colombia (Gonzalez, 1976; FAO, 1978) and has increased even more in Brazil and some countries in the East. In these areas, local companies have begun to produce their own materials. Information from the Caribbean (Pest and Pesticide Seminar Workshop Proceedings, 1980) shows similar increases.

Often even the safest of these pesticides are being used in a manner which threatens the continued safety of the user and the environment e.g. in 1976 in Pakistan, 2,900 persons succumbed to poisoning during spraying of malathion for disease vector control and 5 died (Baker et al., 1977). In other areas, the persistent organohalogens continue to be used for control of malaria and termites. They are also used in agriculture in the Caribbean (Pest and Pesticide Seminar Workshop Proceedings, 1980).

Understandably there are increasing reports of incidences of poisoning and fatalities caused by pesticide misuse. However, in the absence of consistent documentation it is difficult to compile comprehensive statistics based on such reports. In spite of these areas of concern, pesticides will remain necessary in the humid tropics. This section will discuss the major problems which at present impede the implementation of an agromedical approach to pesticide management in humid tropic areas. While there may be at present no simple pragmatic solution to many of these, recommendations will be made for a general strategy which would help reduce the level of exposure of humans to pesticides. The mechanism selected will naturally depend on the peculiar needs and constraints operating within individual territories.



Fishing boat at Sri Lanka

Management of Systems of Agriculture Production

Systems of agricultural production in the humid tropics vary. Mixed cropping of annuals (e.g. corn, beans, aroids) with other crops such as coffee and bananas is usually done on small plot of land (chiefly from 0.2 ha. to 1 ha.). Classical monoculture of sugar, bananas, rice and rubber may occupy larger tracts of land. On coastal plains or in swampy areas adjacent to rice fields, fishing may be a major source of income for entire communities.

Agromedical problems arise from the mismanagement of these systems. The mixed cropping systems are often extensions of the home garden. Many employ traditional non-chemical agricultural practices which can form the basis of a sound integrated Pest Management program (Litsinger & Moody, 1979). However crop husbandry inputs are frequently haphazard and sub-optimal (Haskell, 1977). Depending on the export market or the limitations of the farmer's resources, priority may be given to one crop in the system. Other components are neglected and inadvertently become reservoirs of pest species. Technological information is rarely available on the crop-pest interactions which will allow successful pest management with a minimum essential use of pesticides (Brader, 1979; Smith, 1972). Where pesticides are used, too often this is done on a contingency basis.

Many of these farmers are poor, functionally illiterate and have been exposed to the facility of pesticide use but not the technology which ensures a safe careful selection and application. The level of literacy may not allow clear understanding of the instructions on a label. The result is

Consult physician for
head lice treatment.
Don't do it yourself!

either a combination of different chemicals - irrespective of compatibility - being applied at the same time to crops and livestock alike or the poor selection of a pesticide because it is the only one available e.g. a herbicide being used to control head lice; chlordane or dieldrin which may have been bought for seed treatment or termite control, being applied to a leafy vegetable crop. Such practices naturally contribute to the rapid development of pest resistance referred to in Chapter 4 and the problems associated with this.

In temperate countries, production by monoculture on plantations is often supported by capital expenditure and mechanization which easily generate increased productivity. However in the humid tropics, the continuous production of food in this simplied ecosystem accelerates the rate at which pests reach serious economic levels. Information on economic population indices are not always available and since pesticides are easily afforded, they are used routinely and are considered cheaper than a non-chemical control measure. Equally disastrous is that, in instances where the monitoring system is ineffective or absent, these landowners often import highly toxic materials directly. They may not always be aware of standard practices for ensuring human and environmental safety.

Little is done in most cases to monitor the impact of such use on the ecosystem or to document incidences of poisoning. In several areas of Central or Latin America, cases of poisoning are treated by the specific health service of the landowner and rarely reported. In other countries, the illness or death is often "unexplained" or attributed to another cause.

Applicator Safety in the Tropics

The high temperature and relative humidity in the humid tropics allow persons to wear minimal clothing. Typically spraymen are dressed in the light cotton or synthetic clothing which they may have worn to work, although shoes and shirt are often removed. This increases the risk of exposure to the pesticide but the protective clothing and apparatus now recommended are uncomfortable, impractical and costly. Wearing the denim coveralls, gloves, goggles, respirator and boots in a hot humid environment results in an

Overcome by Heat!

increase in sweat secretion which makes the skin more permeable and increases the risk of dermal absorption. This sweat also tends to collect in the respirator. The applicator further increases the risk of exposure by repeatedly shifting the respirator to remove the secretions. Also, in seeking to be more comfortable, he defeats the purpose of protective clothing by cutting off sections of the coverall, unbuttoning his shirt and finally removing goggles and respirator.

The heavy condensation which may collect on undergrowth and fallen leaves in tropical cultivations also has an effect on applicator safety. The ground becomes slippery. He may move more slowly, depositing unnecessarily large quantities of pesticide on the foliage. Particularly on the slopes where much of the cultivation is done, the applicator is further exposed to a greater hazard as he proceeds with a container of toxic chemical on his back -- he may slip, fall and become covered with the pesticide. Injury incurred may also reduce the speed with which he could seek treatment.

Ecological Considerations

Climatic conditions have a significant impact on the production, efficacy and persistence of chemicals. The development and formulation of new pesticides most often take place in temperate countries. During this development, attempts may be made to duplicate tropical climatic conditions but there are practical limitations to the extent to which compounds are tested under the extreme conditions of heat, humidity, rainfall and intense irradiation which are characteristic of many areas of the tropics.

Chapter 8 describes the ways in which environmental factors limit the effectiveness of pesticides. Some of these will be mentioned again here because of specific problems which are generated. Exposure to intense ultraviolet light, as in extended periods of bright sunlight, increases the rate of breakdown of many chemicals (Freed and Chiou, 1980) including some which are used most frequently in the tropics e.g. malathion. The persistence of the pesticide and therefore its efficacy are consequently adversely affected. Many formulations (e.g. dinocap) even show a greater tendency to cause phytotoxic reactions under these conditions.

Rice paddies in Indonesia

There is also the frequent danger in the tropics of pesticide efficiency being reduced by exposure of compounds to continuous high temperature. Where chemicals are improperly stored i.e. in absence of ventilation, temperatures in the storeroom become even higher than those in the open, thereby reducing the shelf-life of a material. Also during storage, the integrity wettable powder and dust formulations deteriorates under conditions of high relative humidity.

The persistence of a pesticide is clearly affected by the rate and quantity of precipitation. But the greater loss of material caused by excessive runoff from foliage and leaching is a serious source of contamination of the ground water supply. In addition, the abundance of ground vegetation in many areas of the humid tropics reduces evapotranspiration and facilitates heavy runoff during periods of rainfall. Such a source of contamination is therefore a permanent threat. It is compounded where pesticides are misused in those cultivations employing natural irrigaon methods e.g. furrows in sugar cane in the Caribbean, the flood systems in rice in Indonesia, Guyana and Suriname. In these instances, pesticides which are toxic to aquatic life and particularly to fish, help to cause fish kills which often coincide with periods of heavy runoff after rainfall. Although other chemicals may affect levels of mortality, pesticides often play an important role. In many parts of the region, water for domestic purposes is drawn from wells as in East Africa or directly from rivers and streams. The general population is thus unwittingly threatened by another serious source of exposure to pesticides.

Fish kill from leaking drums

There is another dimension to this problem--when the persistence and consequently the effectiveness of a pesticide are reduced as a result of the factors described above, many users of these chemicals try to make ad hoc adjustments by arbitrarily increasing the dosage and frequency at which the pesticides are applied. This is taken also to the point where various compounds may be combined for application at these higher rates and without regard for their compatibility or the effects of this on the level of pesticide exposure to the user, the accumulation of residues in harvestable produce and the contamination of the environment.

Social and Behavioral Considerations

Many instances of misuse of pesticides in the developing countries of the humid tropics can be attributed to specific features of the pervading socio-economic structure. In attempting to relate these two factors, selected examples will be taken from the different points along which a pesticide moves from the system of supply to the system of disposal.

Supply of pesticides

The greater portion of pesticides used in these countries is imported from primary manufacturers and shipped in the form of:

a. the formulated product; and
b. a concentrate which will be diluted at a local formulation plant.

Container consignments are temporarily stored on pallets in warehouse berths at the shipping ports. There have been repeated instances where drums have been pierced by the forklift, bales broken and such damaged containers stored along with the rest of the consignment. Storage space is often limited and berths may be used to house imported foodstuff and pesticides simultaneously. Rarely are special precautions taken to safeguard the loader or the warehouse personnel from continued exposure.

Formulation

Problems with production have recently begun to be demonstrated. Particularly, this is so where the companies involved in pesticide formulation e.g. rat baits or those for livestock ectoparasites are small local entrepreneurs not regulated by the standards of large conglomerates and who are able to operate without the effective control of local authorities. It has been found that some compounds formulated in this manner have resulted in unusual incidences of morbidity and mortality.

Improper pesticide storage on the docks

Distribution

Beware of the dangers of pesticide shops

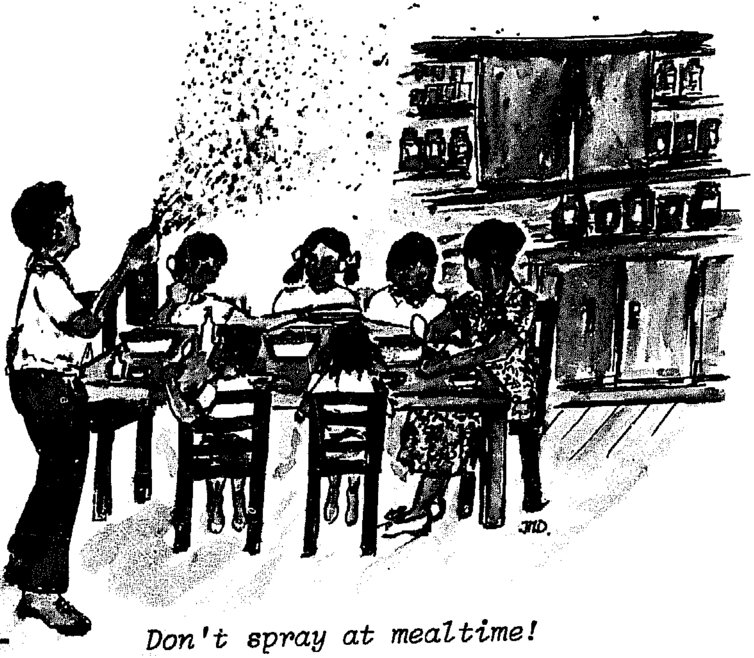
In the greater parts of the tropics, local distribution of pesticides is a largely commercial operation and is often the responsibility of aggressive sales persons having direct contact with the farmers. This has caused the repeated appearance of chemicals which are banned for use in their country of origin and for which there may be safer, more appropriate alternatives. There are repeated instances of the sale of these chemicals at competitive prices to regions which may not have the available information, legislation or the machinery to enforce safety regulations. At times, material has been shipped to the developing countries after the recommended shelf-life has been exhausted.

The significantly lower cost of large containers of pesticides often results in the importation of this type and the need to dispense into smaller, more economical packages for easy distribution and sale. But few local distributors or government storekeepers observe the regulations for safe repackaging. There is often no spout or closed system for dispensing solids or liquids and minimal protection of the operator with considerable spillage and inadquate cleanup. Also, many repackaged containers rarely indicate the strength of the formulated product. This has led to instances of poor selection of product e.g. in parts of Central America, carbaryl is used as a 5% dust for control of livestock pests. When this product was in short supply, farmers substituted the 80% wettable powder formulation and applied it in the same manner with unfortunate results.

Inadequacy of information is also evident in the type of advertising used by many distributors where selective emphasis is placed on specific features of the product. When a popular pyrethrum-based aerosol formulation is advertised as "safe near food," an untrained person often supposes that all aerosol formulations can be treated in like fashion. Recently, there has also been an increase in the sale of small packages of pesticides at the market place without any information other than that offered by the vendor at the time of sale. In addition to other problems, this increases the likelihood of food becoming contaminated with chemicals.

Use and misuse

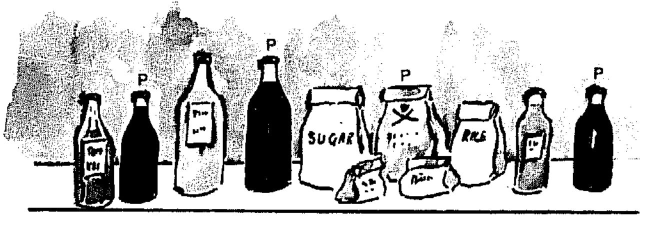
Problems in urban areas of the humid tropics revolve around two features. Urban pest problems e.g. rats, cockroaches and flies are the same as are generated by slum areas anywhere but here they more easily develop to epidemic proportions because of the favorable climate and a frequently inefficient garbage disposal system. Also conditions for storage of food and animal feed in warehouses are not always adequate - commodities are consequently under perpetual attack by storage pests. The demands to control these pests have led to an upsurge in poorly qualified unauthorized pest control operators and many instances of indiscriminate use of pesticides. Repeatedly the convenient aerosol can is used to control flies just before a meal with doors and windows open: the flies escape with a capacity to develop resistance to the pesticide but the food and family are sprayed. An improper formulation of pesticide has often been applied in the warehouses to foodstuff stored in permeable sacks (e.g. sugar, flour). After being accidentally contaminated, the food is repackaged for distribution.



Don't spray at mealtime!

The rural situation poses other problems. More than 60% of the pesticides imported into developing countries is used in agriculture. On a small holding, the farmer combines a number of jobs, he or his family mixes the pesticides, makes the application and is invariably involved in harvesting the produce. The risk of exposure to regular chronic contamination by pesticides is therefore seriously compounded. It is also not uncommon, in the tropics, to find that small farmers enter into private arrangements with the local distributor for the sale of his entire crop. In these situations, there is no clout to food pesticide residue requirements. On other occasions, the crop may be stolen overnight and then sold on the open market probably heavily contaminated with pesticide residues.

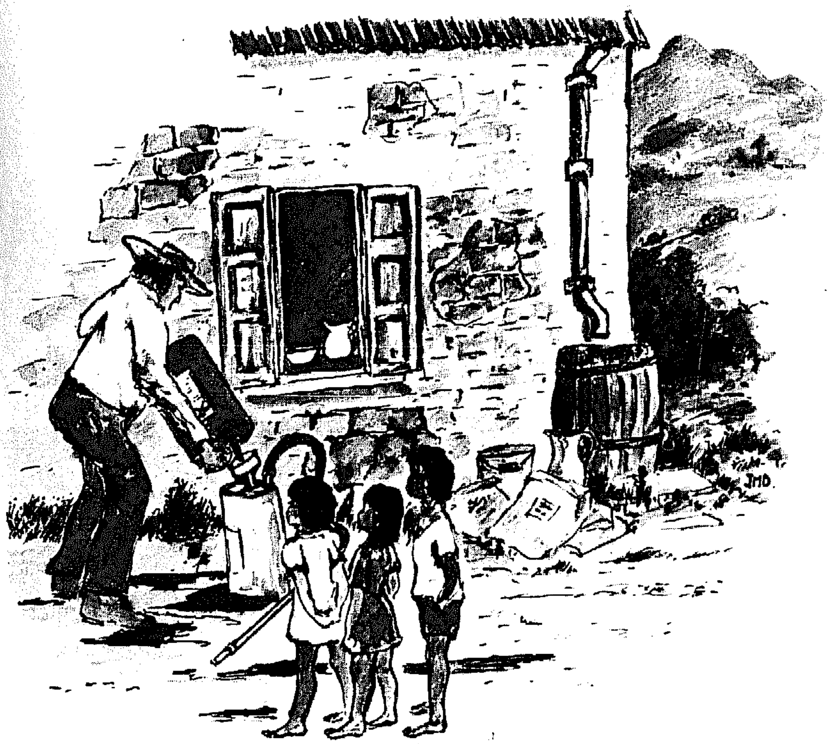
Both pesticides and application equipment have to be imported, are frequently available in limited quantities and at a cost which remains beyond the limits of many small farmers. Pieces of bush are substituted for equipment, dipped in the pesticide mixture, then shaken over the crop. Small quantities of chemical may be obtained from various sources, put into unsafe containers and kept for use. Such storage of chemicals in a haphazard fashion, in unlabeled containers and often near food or foodstuff is dangerous. The appearance of the solid material has allowed it to be mistaken for baking powder or other ingredients in preparing a meal. Similarly, if a liquid pesticide is stored in an alcohol or soft drink bottle - unlabeled and improperly sealed, there is hazard. There are also problems to obtain regularly precise units for measuring and dispensing chemicals. Measurements are often estimated and empty domestic containers, e.g. milk tins, matchboxes, etc. are substituted for measuring and then casually disposed of when the operation is completed.



Pesticides and food should not be stored together

Respirators and goggles are recommended as basic protective devices for the regular user of pesticides. Their effectiveness relies on the closeness of fit. However, many developing countries can afford only the less expensive models with the rigid nosepiece designed for Caucasian features, although in much of the tropics, the majority of pesticide applicators have broader features. Cheaper metal-based cartridges are also less effective since they rust rapidly under the hot humid conditions of the tropics. Replacement cartridge refills are not always available. There may not even be the assurance of continuity in the supply of a particular model. It is possible that the charcoal surgical masks referred to in Chapter 12 may be useful in providing a more universal fit when these have been tested further.

Dispose of measuring cans properly



Don't mix pesticides near the kitchen or children!

Many rural areas have a poorly developed infrastructure including a poorly developed water supply. Water for regular domestic purposes is therefore collected and kept near the kitchen. In many situations, for convenience, pesticides are also mixed in the same location. A single pail used for carrying the water to the home also doubles for mixing the chemical. Often there is spillage. Children may be playing nearby. Empty pesticide containers are popularly used for such water collection.

Limited availability of vehicular or animal-drawn transportation also poses a problem in the tropical orchard or plantation. Fields are traversed by paths which are used by the general population, especially school children, who are seldom aware of the danger of an on-going pesticide application. Many times they may be intrigued by the appearance of new technology. There are serious dangers of chronic exposure through inhalation, dermal contact with foliage or food. The threat of exposure through volatilization of a pesticide is greater here than in a temperate region (Chapter 14).

The inadequacy of the transportation system also affects the prompt transfer of a suspected poisoning case to a treatment center. Invariably rural areas are far from the few general hospitals and are serviced by health centers which operate only during limited periods of each day. They are also staffed by persons who have not been trained to recognize pesticide poisoning symptoms and to distinguish between those caused by compounds requiring specific treatments. Antidotes are rarely available at these centers.

Don't spray near the school bus stop or groups of children!

Pesticide Protection Stategies in the Tropics

Policy-making bodies within tropical countries must recognize and act upon their responsibility to ensure that the increasing potential threat to the safety of their environment be reduced. International standards must be considered in relation to the specific requirements of tropical countries. In so doing, relevant intermediate technology could be developed. The peculiar needs for increased pesticide protection revolve around developing systems for:

1. Legislation: to formulate and implement practical measures which will ensure safe use of pesticides within the context of available resources;
2. Information: to increase and maintain a source of information on pesticide use for tropical conditions;
3. Education: to develop and train technical persons and the general public in their own responsibility for human and environmental safety.
4. Agromedicine: to extablish a core agromedical infrastructure which will ensure that human and animal exposure to pesticides is minimized.

Legislation

Clear comprehensive legislation and regulatory processes (FAO/WHO, 1969) are vital as the basis for the control and monitoring which tropical countries need to do to sustain a proper program of pesticide protection. An infrastructure must be developed to enforce the regulations desired. These processes must ensure:

1. Strict control of the quality, safety and entry of pesticide products used within a territory.
2. Observance of clear guidelines for proper storage of chemicals and treatment of foodstuff in warehouses and supermarkets.

3. Registration and certification of all pest control operators after these have satisfied basic requirements of training.

4. Compliance with all safety regulations for workers by manufacturers or distributors of pesticides within the region.

5. Development of a system of inspection for urban and rural areas to ensure that regulations are being followed. Penalties must be imposed for any infringement of the law.

6. Establishment of policy directed at maintaining the necessary research programs which would provide local information on effective rates and times of application as well as residue limits.

7. Control of the manner in which media advertising is used to promote sale of pesticide products. Information thus released must comply with guidelines for pesticide protection.

Information

Information must be provided through research to allow pesticides to be selected and used correctly. Mechanisms must be set up and maintained for:

1. Effective dialogue and cooperation between government, industry and universities and other regional and international organizations.

2. Development of a system to safeguard the territory from self-interest in the chemical manufacturing industry. A limited number of select comprehensive laboratories could be established with the resources necessary for confirmation of the levels of contamination and regular quality control analysis of different formulations of a product.

3. Field testing of formulations by researchers under conditions which more closely represent tropical extremes. This will determine the effective modes of formulation e.g. an encapsulated dust or granular product which resists ultra-violet degradation for a longer period; the selection of effective adjuvants to ensure a more lasting retention of pesticides on foliage in areas with heavy precipitation.

4. Establishment of the precise rates and intervals for application of the compounds most frequently used. The relevance and duration of re-entry risk intervals will change dependent on the rate of breakdown of a product in a humid tropical environment.

5. Development of simple, rapid and relatively inexpensive analytical tools e.g. thin-layer chromatography to expedite monitoring of pesticide residue contamination.

6. Development of light protective clothing suitable for use in the humid tropics similar to that described in Chapter 12 and a safe practical method of container and chemical disposal, adapted from the one outlined in Chapter 15.

7. Structuring research policy to facilitate the development of effective pest management programs which relate to the specific systems of production used in the humid tropics.

8. Establishment of a mechanism for preserving a history and record of pesticide use, exposure and incidences of poisoning and treatment.

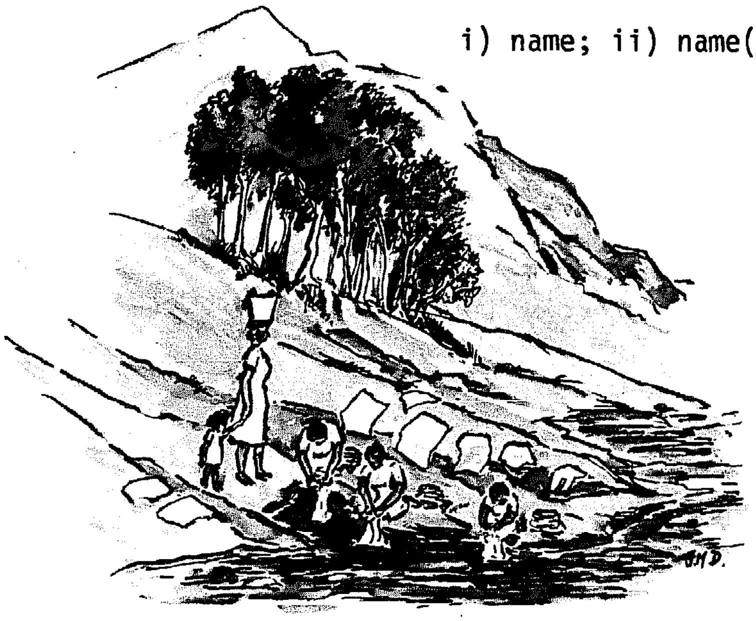
Education

Education is a continuous process and would involve training at three levels viz., technical personnel to advise on handling of pesticides and treatment of cases of exposure; applicators and the general public on the safe, proper use and disposal of pesticides. A viable program would ensure the development of prophylactic measures to reduce the degree and incidence of misuse as well as the correct diagnosis and treatment of pesticide poisoning cases.

Some measures to be taken are:

1. Maintenance of standards to ensure the safety of the operator by
    a. encouraging operator's use of protective apparatus by educating them to the danger and making the use of such protection a requirement of employment;
    b. providing all regular users of pesticides with tags to be attached to the coveralls bearing the following information:

       i) name; ii) name(s) of chemicals used; iii) antidote.



    c. establish a system where protective clothing remains at the farm and is laundered there. Where this is not possible, explain that such clothing should never be washed in a river or pond. Exposure to sun after laundering also increases the photochemical breakdown of a pesticide (see Chapter 12) and consequently the amount of residue which remains. Operators must also be encouraged to shower before returning home.

2. Training in the correct method for mixing and applying pesticides as described in Chapter 13.

3. Protection of other persons and the environment by ensuring-
    a. Safe separate storage for chemicals. Keep these away from human or animal food or where children may have easy access.

b. All chemicals to be kept away from natural water sources e.g. by the use of closely-planted buffer strips of a crop e.g. grass or short legume which helps to trap excessive run-off of the pesticide into the water. Where a river or pond is the nearest available water source, it is better to collect water and carry away from the source for mixing pesticides than to leave the pesticide container near to the waterway.

c. Proper disposal of all containers used in a pesticide operation e.g. where orthodox calibrated utensils are difficult to obtain, a more economical local substitute can be constructed that is VISIBLY different from a food container. Empty pesticide containers should never be used for other purposes e.g. holding water or collection of garbage. Perhaps chemical companies could cooperate by encouraging the return of larger containers.

Agromedicine

Establishment of a core agromedical infrastructure would provide the essential instrument used to achieve the common goal of increased human health and productivity. It would ensure that the dangers associated with pesticide exposure are minimized and correct prompt treatment is given in the event of poisoning and should involve:

a. Regular training of health personnel to ensure proper recognition, treatment of pesticide poisoning victims and maintenance of a record.

b. Training at least one influential member of the rural community e.g. the village headman, to recognize symptoms of pesticide poisoning and the steps for FIRST AID.

c. Consolidate this by general public education.

d. Devise a system for transport of a victim of pesticide poisoning to the nearest resuscitative resource (clinic, doctor, nurse, etc.) in the case of a human or treatment and quarantine in the case of animals.

e. Establish at least one functional accessible poison information center in a country and publicize its role.

II. The Public Health Perspective

by Alfred A. Buck

Geographic Variations of Disease Patterns Related to Agromedicine

Agricultural development is closely linked to changes of the prevalence, distribution and severity of important endemic diseases, notably malaria, schistosomiasis (snail fever), trypanosomiasis (African sleeping sickness, and Chagas' disease in Latin America), leishmaniasis (oriental sore, kala azar, "Uta," etc.), filarial infections (lymphatic filariasis, onchocerciasis or "River Blindness," loiasis, etc.) arbo-virus infections and hookworm disease. With the exception of hookworm infestation all of the above diseases involve either arthropod vectors or intermediate snail hosts (schistosomiasis) in the life cycles of their causative agents. Changes in the environment, brought about by agricultural development projects, can have pronounced effects on endemicity levels of the major tropical diseases in a number of ways. In man-made water impoundments and irrigation projects, there is usually an increased opportunity for the arthropod vectors of disease and the snail hosts of schistosomiasis to breed. Irrigation systems extend geographically over wide areas, causing rapid spread of breeding sites of vectors and opportunities for more frequent water contact of rural people to snails infected with schistosomiasis. The same changes of the environment may have negative effects on the epidemiology of other diseases, especially on onchocerciasis whose blackfly vectors need fast-flowing rivers and streams, rapids and turbulence to meet requirements for high oxygen concentrations of its *Simulium* (blackfly) vectors.

Construction of roads, deforestation, creation of gallery forests, and game reservations have caused ecological changes conducive to outbreaks of African sleeping sickness. In South America, the rapid building of primitive adobe houses with thatch roofs for new settlers in development projects has produced favorable conditions for the proliferation of the "kissing bug," *Triatoma infestans*, the vector of Chagas' disease.

Rapid increases of rodent populations in semi-arid areas, including the fringes of new cities and towns under construction, may give rise to intensive transmission of leishmaniasis by sandflies (*Phlebotomus*). Biological adaptation of vectors and snails to breeding conditions prevailing in certain periurban areas of the tropics and even within urban areas themselves have led to the new phenomenon of urban filariasis, and in some parts of Africa, also of urban schistosomiasis (*S. mansoni*).

The epidemiology of the major endemic diseases is also markedly affected by large-scale migration of new settlers and seasonal laborers to newly developed agricultural areas. Among the population groups attracted by these economic opportunities are many persons who are infected with tropical parasites and who may seed new foci of the infection in hitherto non-endemic areas. On the other hand, there are migrants who have had no contact with these infections and who make up a large body of susceptibles in the population. This combination of factors may cause an explosive situation; the epidemic increase of urinary schistosomiasis after the creation of the Volta Lake is a good example. In many tropical countries of the world, especially in Africa, multiple infections with the agents of major tropical disease are the rule rather than the exception. A single vector species can transmit more than one disease, i.e., malaria, filariasis and arbo-viruses; vectors of different disease may breed in the same water bodies (malaria and schistosomiasis); other vectors of disease, although different in their biological requirements, may overlap in their vectorial range and capacity and affect the same community.

An example of the phenomenon of "co-endemicity," i.e., the co-existence of different diseases in the same area is shown in Figure 20-1 for Africa. Because people have multiple infections, there is disease interaction. This, in turn, may influence the tolerance, bioavailability, metabolism and pharmacokinetics of drugs used for treatment of patients. These factors can also influence the degree of toxicity of pesticides and molluscicides to persons who are living in areas where these chemicals are applied to crops or for disease control.

There are large variations in the spectrum of diseases between different communities. Because of dissimilarities of disease patterns it is difficult to make extrapolations from the findings of a small, well-studied population to a large area. Even within the population of a single village with a characteristic disease spectrum, there may be pronounced differences in the frequency and severity of individual parasitic infections. Figure 20-2 and Table 20-1 summarize the findings from a community where onchocerciasis and two types of schistosomiasis, S. mansonia and S. haematobium, are co-endemic. This combination of parasitic infections is affected by the distance of the residences of the villagers from the Lim River where Simulium damnosum, the local vector of Onchocera volvulus, breeds throughout the year (Figure 20-2). Residents living close by the river have the heaviest skin infections with microfilariae of O. volvulus and the highest frequency of microfilaruria, a complication associated with heavy loads of infection, but they have little intestinal schistosomiasis. Throughout the year, the Lim River remains the only water supply for this segment of the village population. In contrast, residents living at a greater distance from the Lim River try to ease the arduous task of fetching their daily water supply by using the nearby Mbongo Creek which harbours Biomphalaria snails and provides ample opportunity for transmission of S. mansoni but has no Simulium breeding. During the dry season when the water of the creek becomes unsuitable for domestic use the villagers have to go further away to the Lim River. These differences in water hauling practices have led to relative differences in the frequency and intensity of the two infections within the village. All infections with S. haematobium have been acquired at fishing places outside the village and are unaffected by the different types of water supply in the community (Buck, et al., 1978).

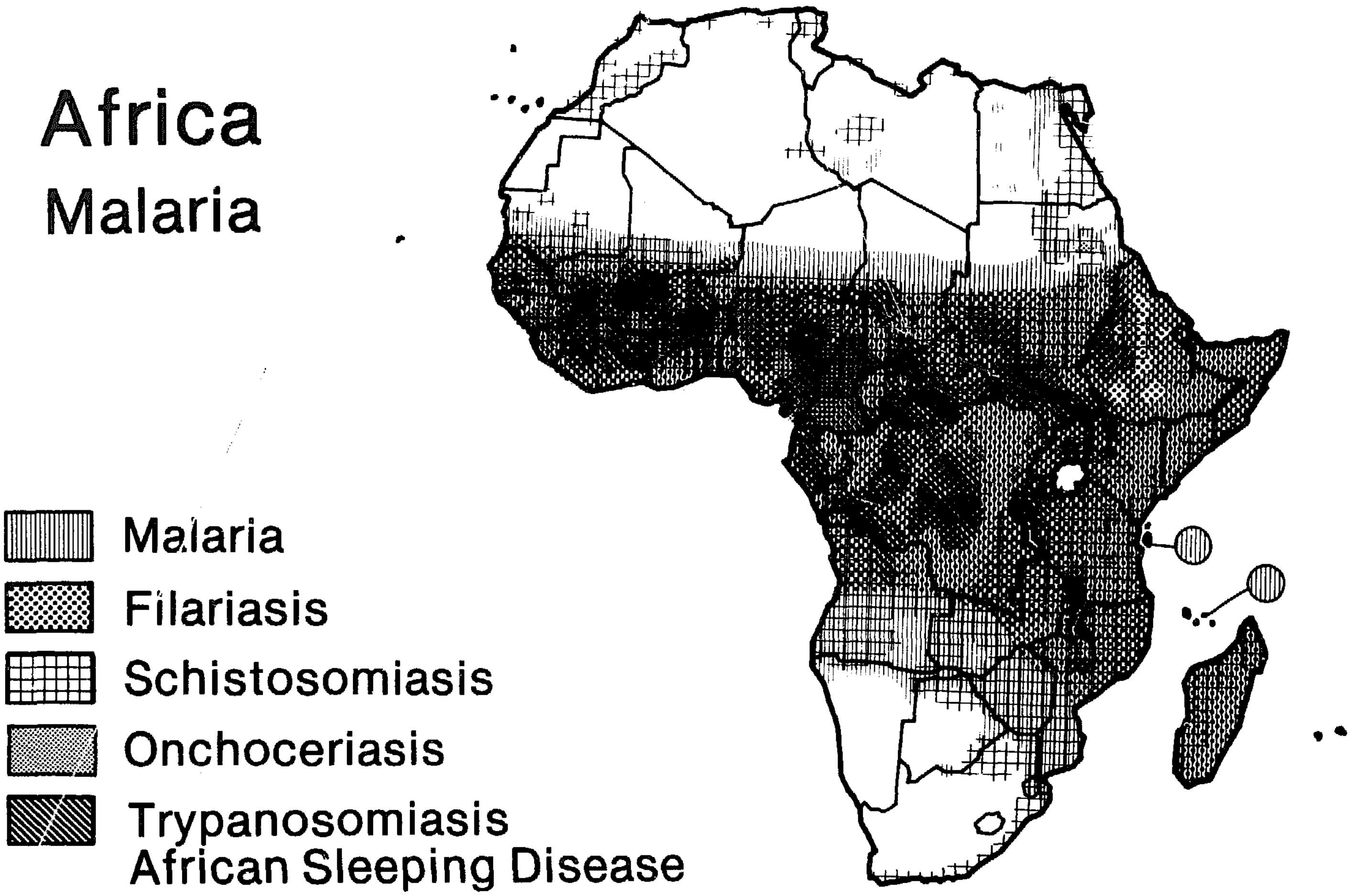
As regards to pesticide management in less developed countries, there are certain specific interactions with medical projects of disease control and treatment.

1. Risk Factors Affecting Disease Control Strategies

Elimination or reduction of vectors through application of pesticides (adulticides and larvicides) is an essential part of disease control. The application of specific insecticides for disease control is usually focal, either as residual spraying of houses or as application of larvicides to the breeding place of vectors. In contrast, the use of pesticides to crops usually covers a large area. Although quantitative estimates of the effects of agricultural pesticide use on resistance patterns of local disease vectors are not available, field experience has shown that such interference may be significant. For

Figure 20-1.

Areas of co-endemicity of major tropical diseases in Africa[1].



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[1] Based on the most recent epidemiological data published in expert committee reports of the World Health Organization.

example, in the Qunduz Province of Afghanistan the original local malaria vector, *Anopheles superpictus* has disappeared as a result of 10 years of systematic vector control. Instead, two relatively unknown mosquitoes have benefited from the changing ecology which was partly the result of agricultural development and partly the effect of malaria control. The extension of irrigated rice and melon fields in the area combined with the generous use of pesticides for malaria and pest control has led to biological adaptation and selection of two different mosquito species which have since become new vectors in the local transmission of malaria. Over the years, the first of the two new vectors, *An. hyrcanus*, has developed resistance to DDT and other insecticides, while the second, *An. pulcherrimus*, although still susceptible to pesticides avoids resting on surfaces treated with these chemicals. Moreover, the two mosquitoes are exophilic and, unlike the original malaria vector *An. superpictus*, are not much affected by residual spraying of houses. While these developments have taken place, little has changed in the personal habits of the indigenous rural populations. Most of them still spend hot summer nights sleeping out-of-doors without any protection of mosquito nets.

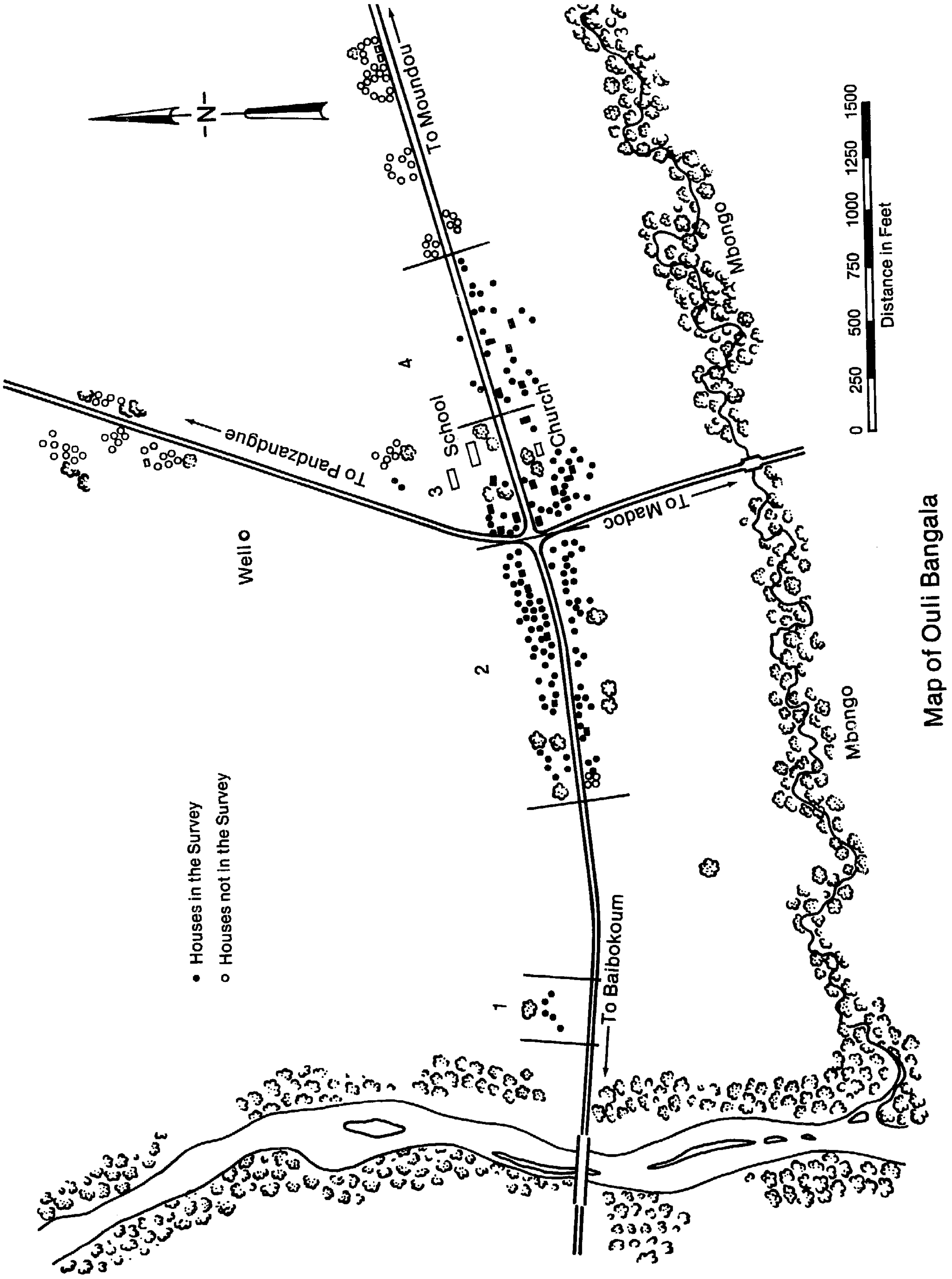
Table 20-1. Prevalence of Infection with *O. volvulus*, *S. mansoni* and *S. haematobium* and of Onchocercal Microfilaruria by Types of Water Supply and Distance of Residence from *Simulium* Breeding Site, Ouli Bangala, Chad

	Location of Houses: Distance from Lim River			
	100-200m Zone 1 N=35	450-800m Zone 2 N=197	800-1,000m Zone 3 N=88	3,000m+ Zone 4 N=66
Use of Mbongo for water (%)	NONE	50	57.2	66.7
% *O. volvulus*[1]	85.7	85.8	79.5	
72.7				
% microfilaruria	20.0	12.7	9.1	6.1
% S. mansoni	13.0	48.4	47.5	45.8
% S. haematobium	9.3	5.9	7.1	6.1

[1] Percentages are age-adjusted.

Figure 20-2.

Location of houses by distance from the Lim River (Simulium Breeding) and the Mbongo Creek (Biomphalaria snails), village of Ouli Bangala, Chad.[1]



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[1] A. A. Buck, et al., Health and Disease in Chad, The Johns Hopkins Press, Baltimore, Maryland, 21205, 1970.

2. Risk Factors of the Human Host

In addition to primary toxicity of the pesticides as discussed in more detail in other chapters of this book, there are a number of important factors related to pesticide use that can influence the symptoms of a disease and drug tolerance. Chemical compounds similar in structure to those used for agricultural pest and snail control are also administered for medicinal purposes, especially for treatment of schistosomiasis and tapeworm.

A new drug used in the chemotherapy of urinary schistosomiasis is metrifonate (Bilarcil®). This organophosphorous compound (o,o-dimethyl-2,2,2,-trichloro-hydroxethyl-phosphate) suppresses cholinesterase activity in the plasma and the red cells. Multiple exposure of patients under treatment with metrifonate to other phosphoric-acid esters or similarly acting compounds can lead to potentiation of cholinesterase inhibition and cause serious side affects. Such double exposure may occur in patients who handle or come into contact with compounds used for plant protection, pest control or anthelminthic treatment of animals.

The drug of choice for treatment of tapeworm in man (_Taenia saginata_ and _T. solium_) niclosamide (Yomesan®). The same chemical substance is also used for snail control under the name of Bayluscide® and in veterinary medicine. Large scale and regular application of molluscicides for snail control in schistosomiasis projects has been in use for many years in Egypt, the Sudan, and other parts of Africa. Little is known as yet about the possible effects of consuming water contaminated with niclosamide on reducing the prevalence and distribution of taeniasis in man and domestic animals.

In areas where different types of pesticides are applied regularly and in large quantities, the indigenous population may be exposed to risks that might aggravate the clinical manifestations of an endemic disease, especially schistosomiasis and of possible interference with the immune systems of persons chronically exposed to pesticides and their metabolites in the environment, food and water.

Similarly, the observed variations of the efficacy of specific types of chemotherapy and of the frequency and severity of untoward side reactions need to be examined in relation to the degree of exposure to pesticides in the population.

In medical ecology, the ever changing constellation of host and environmental factors in development projects can influence the natural history of disease. These changes need to be monitored and studied by multidisciplinary teams. The epidemiology of pesticide use, including their effects on individual diseases and on local disease patterns, require careful consideration in agricultural development.

III. Persistence of Chemicals

by Carroll Collier

Degradation of pesticides in any environment is mediated by photolytic, hydrolytic, enzymatic (plant and animal), microbial and catalytic processes. Of these, hydrolytic, enzymatic and microbial processes are temperature dependent and therefore are potentially more rapid in hot climates where the mean soil and air temperature are higher than in temperate zones. Likewise photolysis of pesticides on soil and vegetative surfaces and in the upper several meters of water in lakes and streams can be expected to be more rapid in tropical or arid zones exposed to high levels of actinic activity.

Additional and significant losses can occur through the process of volatilization and this increases in areas having high average soil and air temperatures. A final means of loss is that which occurs by the process of co-distillation. Here again, high temperatures accelerate the process.

Recently several authors have concluded that the use of persistent pesticides in the hot humid tropics may be safer than in temperate zones due to a much more rapid rate of degradation.

Sleicher and Holdcraft, (1979) in studying the persistence of DDT in surface soils in Kenya found that the rate of disappearance of DDT from soil near Lake Nakaru, Kenya gave a half-life of 100-200 days. They attributed this rate to sublimation and concluded that "uncontrolled use of DDT in Kenya may affect wildlife to a lesser extent than had been feared." They estimated for half-life in an exposed plot a value of 100 days and for a shaded plot 200 days. However, in these experiments the DDT was sprayed onto vegetated spots which were undisturbed during the course of the experiment, conditions which are quite different from those where DDT is applied to an agricultural crop and subsequently incorporated into the soil incidental to plowing and tillage. Hence these extremely short half-lives primarily attibuted to loss by sublimation may be more indicative of the rate of loss from exposed surfaces than from soil which has DDT incorporated therein.

Talekar et al. in 1981 studied the persistence of five insecticides in subtropical soils after repeated applications over 5 years. They concluded that precipitation and temperature appear to be important factors for rapid degradation and that degradation was faster during hot and rainy months and on cultivated land as contrasted to fallow soil. DDT and dieldrin were applied at 5 kg ai/ha each spring and fall for a period of four years. In the case of DDT over the four year period, no buildup occurred.

After the first two years, however, residues of dieldrin increased with each application. Close inspection of the degradation curves suggested that regardless of whether a buildup did or did not occur combined residues of DDT and DDE in such soils could be expected to be at environmentally significant levels for a number of years following complete cessation of use.

Sethunathan et al. 1980, concluded that under certain conditions, tropical soils of high organic content under flooded conditions (anaerobic) can degrade many of the chlorinated hydrocarbons, including DDT very rapidly. Persistence values of less than 90 days were noted for several soil types.

However, certain soils were encountered where degradation, even under the above stated conditions was no more rapid than in temperature climates.

Even though a strong case can be made for the relatively more rapid rate of degradation in the hot humid tropics due to the combined effects of increased temperature, sunlight and microbial activity the overall rate of decline is not sufficiently rapid so as to prevent problems with residues in food, human body tissue and wildlife.

Pesticide monitoring studies of chlorinated pesticides in human tissues conducted in developing nations, where the climate is either hot-humid or hot-semi-arid, in general show much higher levels of pesticide residues than in developed countries.

Likewise pesticide monitoring studies conducted in tropical areas tend to show average residue levels of DDT in the same order of magnitude as found in similar studies conducted in temperate zones. For example, if one compares the residue levels of DDT, DDE and dieldrin found by Greichus et al. (1978 and 1978a) in fish from lakes in Kenya and Zimbabwe with that summarized by Edwards, 1973 from developed country monitoring studies it can be seen that the data on the average are comparable.

Unfortunately there is all too little residue monitoring data from developing countries (WHO, 1980) and that little which does exist is used extensively in deriving broad conclusions.

If the pesticides are bioaccumulative, such as exemplified by many of the chlorinated hydrocarbons, residues of these chemicals can be expected to enter critical food webs regardless of whether the pesticide is highly persistent or even moderately persistent.

Another item worthy of mention is that of "buildup" of persistent pesticides. It can be calculated, (Hamaker, 1972) that for most pesticides, including even the chlorinated hydrocarbons, with typical seasonal applications, the absolute maximum level of pesticide present will never exceed a fixed quantity. For example, for a pesticide with a half-life of one year, if one applies single annual dosages of 1 pound per acre of pesticide the maximum residue level which could ever exist would only be 2 times the annual rate of application or 2 pounds per acre!

Another item for consideration is the concept of Wheatley (1964) who concludes that the half-life of a pesticide in soil is logarithmically related to time after initial application. This affirms much of the current data in soil persistence studies wherein high initial loss phases (first half-lifes) are succeeded by successively slower rates of degradation (later half-lifes). If this is true then even after total cessation of use of a persistent pesticide, lingering low-level residues could be expected for many years in the future.

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Chapter 21

Implementation of Agromedical Concepts

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SUMMARY

Previous chapters have dealt with specific concerns in agromedical programming. This chapter attempts to summarize some of the techniques and ideas for integration and implementation of these practices in a holistic program. Particular emphasis is given to the development of an agromedical organization appropriate to the needs, the laws, and the resources of the country.

The essential ingredients include a) a knowledge of integrated pest management and a work force which is knowledgeable on all of the alternative tactics for pest management, b) a regulatory system that is reasonable and enforceable, c) an efficient analytical capability, and d) an interdisciplinary agromedical infrastructure.

INTRODUCTION

Previous chapters have introduced the agromedical concept (Chapter 1), described pesticides (Chapter 2), dealt with the acute and chronic toxicity of pesticides (Chapters 6 and 11), and a variety of other topics related to pesticide management by the agromedical approach. Chapter 1 particularly attempts to illustrate the inseparable relationship between agriculture and medicine in assuring a healthy productive populace. The collaboration of these two important professions is essential in the area of pesticide management. The huge number of pests that debilitate man and limit agricultural productivity require effective action. Pesticides are among the several tactics available for pest management and because of their effectiveness and immediacy of action have been widely used. Pesticides, however, are highly sophisticated technological tools (NAS, 1975 and U.S. Department of State, 1979) that require regulation and appropriate knowledge to be used in a manner that is safe for both man and his environment. The properly implemented agromedical approach assures this.

The knowledge and skills inherent in the agromedical approach and the infrastructure of human and physical resources that go to make it up have an application beyond pesticide management. The capability exists to be applied to other chemical problems. Thus, the agromedical capability can be applied to problems of regulation, transport, storage, handling, and disposal of industrial and other chemicals as well (NAS, 1975b). It thus becomes a valuable and effective resource to the nation.

TACTICS FOR PEST MANAGEMENT

While this book emphasizes the agromedical approach to pesticide management, sight should never be lost that pesticides are not the only tactic available for control of pests (Bottrell, 1979; NAS, 1975a; and OTA, 1979). In fact, the properly focused agromedical approach will emphasize the employment of all the different pest-management tactics in the most economic and ecologically sound system. This may involve the use of several different tactics in a combined Integrated Pest Management (IPM) program or Integrated Pest Control (IPC). In certain instances, because of the nature of the pests, the crop and physical conditions, a more limited array of tactics or methods may have to be employed (Apple and Smith, 1976). Again, on occasions, there will be instances where chemicals will be the only available method for control of a pest. It is important, however, for the agromedical team, or perhaps the individual working at a village level, to be aware of the many methods of pest management that can be applied for different purposes. In integrated pest management, it is assumed that each pest species in a cropping ecosystem has a population level below which there is no economic injury. IPM rejects the idea that mere presence of a pest species justifies actions for control. In fact, maintenance of low levels of some pests may be a desirable management practice. When the pest population levels threaten economic injury, then remedial actions are taken. The objective of good pest management practice is to maintain the pest population at non-injurious levels.

It is important in integrated pest management to recognize the agroecosystem as the management unit (Apple and Smith, 1976). Any manipulation of the agroecosystem, i.e., the cropping system, may aggravate pest populations on the one hand or effectively manage them on the other. Manipulation with no apparent direct effect on the pests may have subtle, indirect, or secondary effects of great significance. The change to a new crop variety, rotation to another crop, change in fertilizer, modified row spacing or irrigation schemes, change in pesticide use patterns and other manipulations may cause a drastic shift in the status of a pest species or its natural enemies. These management tools, if utilized properly, can be the means of keeping the pests at non-economic levels.

The choice of the method or methods to be employed in pest management requires that we know what the pest is, something about its nature, the threat that it poses, whether or not a certain level or population of the pest may be tolerated, and whether or not it has natural enemies that can be utilized in the control program. Beyond that, there needs to be a recognition of the ecosystem or area in which the organism breeds and lives, and the impact of the proposed control measures on that system. Consideration also has to be given to the possible impact of the control measure on humans.

The four primary tactics (Bottrell, 1979) utilized in integrated pest management are:

Host resistance

Over many thousands of years, crop plants and animals have been selected for resistance to pests. Even partial resistance can be utilized in a pest management scheme. Farmers' traditional varieties are often a source of such resistance and new lines of resistance can also be incorporated in otherwise suitable crops by breeders.

Cultural controls

A large variety of crop and animal management practices provide the subtle or secondary effects useful in pest suppression. Cultivation may destroy breeding habits or impact directly the pest population. Plowing or other destruction of crop residues may deny the pest an overwintering or breeding habitat. Crop rotations can break up continuous breeding of pests and may have other benefits. Adjustments in fertilizer and irrigation practice also can be utilized in pest management.

Natural controls

In addition to natural enemies, a variety of ecological factors inhibit increase of pest species, e.g., limited resources, inclement weather, and competition with other species. These can be utilized in pest management; the goal is to alter the pest environment to enhance the action of natural forces. The procedures may entail conservation and augmentation of resident natural enemies, introduction of new natural enemies, and other environmental manipulations.

Chemical methods

There are a variety of chemicals that can be used in pest management. There are, of course, those chemicals that kill the pest outright, including synthetic chemicals, those of botanical origin, viruses, and bacteria. In addition, however, there are chemicals that may be used as attractants to lead the insects away from the crop to be protected; repellents, chemicals that inhibit the growth of insects, or plants and chemicals that result in sterilization, making the organism unable to reproduce.

Any control procedure may produce unwanted or objectionable effects. In integrated pest management programs it is very important to be alert for such undesirable effects and avoid them. An example of such undesirable effects would be the destruction of an important enemy of one pest from the use of a pesticide in the ecosystem for the control of another one.

LAWS AND REGULATIONS

Pesticide management begins, of course, with the appropriate law and regulations established at the national level (NAS, 1980). However, as pointed out in an earlier chapter, these laws and regulations should be drawn with a view of the capability for implementation and enforcement. A detailed law that is unenforceable is of little worth. The laws and regulations should be based on achieving the most important ends, namely that of protecting humans and the environment while at the same time facilitating pest management and agricultural production. There are times, of course, when such laws also are drawn to encourage the development of local industry.

Laws and regulations generally deal with what chemicals may be imported or manufactured, requirements that they be handled in such a way as to minimize hazards and provide for the proper use on the designated problems. Beyond that, the laws and regulations will specify residue levels that are acceptable, to whom the chemical may be sold, and the purposes for which it may be used. Appropriate labeling will be a part of this regulatory document.

Analytical capabilities

Effective implementation of pesticide regulations requires the ability to analyze for the chemical. This means having the capability of analyzing the technical product and the formulated product to assure that they meet label standards; also possessing capability of analyzing for residues, in food, water and other environmental samples and analyses for breakdown and byproducts for contaminants. Therefore, any regulatory scheme must provide for establishment of a chemistry laboratory with analytical capabilities. In addition, there is need for sample collection which may be done by laboratory staff, agricultural and health inspectors, or other governmental agency personnel (Document PB 377, 1980; NAS, 1975a; U.S. MAB, 1979; NAS, 1980; WHO, Technical Report NO. 513, 1980).

As pointed out in Chapter 18, not all laboratories involved in pesticide management need have the most expensive and sophisticated equipment for analyses. Very often, simple inexpensive methods of analyses such as thin-layer chromatography, spectrophotometry, or even bioassay, will provide satisfactory answers as to the quality of the product or the residue level in a given sample. Where manpower and monetary resources are scarce, consideration might be given to establishing a few primary laboratories with thin-layer chromatography and/or bioassay capabilities, should be established with one national laboratory that has more sophisticated and sensitive equipment.

THE AGROMEDICAL INFRASTRUCTURE

There is probably no single best way of organizing the agromedical infrastructure for pesticide and chemical management. The organization should be adapted to the needs, customs, laws and resources of the country. However, there are certain features that are probably desirable in the organization such as a national level committee, board or commission comprised of representatives of agriculture, health, manpower, transport, and of course, law. In addition, such a board or commission will need appropriate scientific advisors from such disciplines as public health, entomology, toxicology, environmental science, chemistry, agriculture, and others.

The responsibility of the national committee, board, or commission would be to coordinate activities and information among the various ministries and agencies, review the information on pesticides that may be imported or manufactured in the country, appropriate labeling, and other aspects of pesticide management. Such a national group would also be concerned with training programs, both short-term and long-term, and coordinating the entire agromedical infrastructure down to and through the village level. In addition, they would consider what pesticides are used; how and where such pesticides are used; transport, storage and disposal problems with chemicals. Further, they would be concerned with the establishment of capabilities for first aid in case of poisoning; through more elaborate medical capabilities and matters of environmental protection. Such a board or commission would also deal with the matter of establishing regulatory laboratories as well.

Some of the specific responsibilities of the national group would include:

1. Planning, direction, and administration of the agromedical programs in coordination of the effort of the various agencies and interests;
2. Direction and support of the technical activities and research;
3. Collection and evaluation of statistics on agromedical data;
4. Development of laboratories and laboratory services for monitoring food, feed, humans, the environment, and technical products (in addition, they would maintain a national quality assurance program for the laboratories); and
5. Develop a program of public information to acquaint agriculture, industry, health, and agricultural workers and the public with safe pesticide usage and effective pest management programs.

At the state, regional, or departmental level, the agromedical team or committee need not be as large or far ranging in their responsibility. This group probably would focus more intensely on implementation of the program designated at the national level. To be sure, such a committee would, in turn, often have valuable suggestions and information for the national group.

The responsibilities of this level might include:

1. Supervision and follow-up of the work of committee officials at the local level;
2. Receive reports, compile and evaluate statistics and, based on this information, develop appropriate recommendations for practices and procedures for safe, effective use of pesticides;
3. Have primary responsibility for the development and arranging of training programs responsible for agromedical practices (this would cover such topics as integrated pest management, hygiene, disposal of chemicals, and nutrition);
4. Provide recommendations for appropriate regulations for pesticide applicators;
5. Conduct investigations of any problems that may arise; and
6. To the extent possible, carry out monitoring and medical surveillance programs for protection of human health and the environment.

At the local and district level, the agromedical team may be quite limited in size, in fact it may reduce to the activity of one or two people representing agriculture and health. In some instances this may be the local medical officer and agricultural extension agent, or could be a community leader that has been designated to represent the agromedical team at that level. In some countries, the practice has been developed of identifying a village or district leader whose integrity and knowledge encourage people to seek his advice. Such an individual with basic training in the agromedical approach to pesticide management, hygiene, and other relevant topics could provide the advice and counsel needed for safe, effective use of pesticides, encourage the development of economic, environmentally sound pest management programs, and possess the basic knowledge needed for first aid in the event of an accident. The individual should have ready access to a medical services facility so that in case of emergency, the victim or victims could receive prompt medical attention.

Thus, the responsibilities at this level would involve:

1. Teaching and advising farmers and other pesticide users concerning the appropriate agromedical practices in agriculture and health with reference to pesticide management, control measures, nutrition, and avoidance of poisoning;
2. To deliver first aid to poisoned individuals including the use of simple antidotes (see Chapter 7) and then to forward the individual to the proper place for more advanced medical treatment;
3. Do preliminary investigation of incidents of poisoning;
4. Do some collection of samples for analyses, including food and water, and other environmental samples.

The structure of the agromedical effort need not be unduly costly or elaborate providing that the cooperation of ministries, universities, and others is given in support of the program. Resources are not always available to establish a large research and regulatory effort to develop all the data necessary for pesticide management within the country. In this case, the use of data and information from other countries, plus data available from within the country, if analyzed and applied to the local conditions by the scientists of the national board, may achieve the desired ends. As indicated previously, such a practice is being followed at the present time in certain countries with seemingly satisfactory results.

Conclusion

We have attempted to provide a background information for the agromedical teams and individual workers to develop practices that protect the public, the workers, and the environment from adverse effects of pesticides. Of particular importance in value in this activity area is continuing training and educational efforts. It is probable that as people understand more of the chemical world in which they live, and the nature of the chemicals they use, the safer will be their practices. For example, in manufacture, use, and disposal of chemicals, they will be more cognizant of hazards to themselves, to the environment, and to water supplies from improper management. Therefore, following some of the practices outlined in the aforementioned chapters plus appropriate adaptation to their own situation will help to avoid untoward consequences.

It is hoped that this book, will provide stimulus for the generation of ideas in implementing agromedical practices. These practices, as pointed out, apply not only to pesticide management, but can also be beneficial in managing other chemical problems. It is believed that the ingenuity evidenced by people once given the germ of an idea will enable them to develop technology appropriate to solve their own problems.

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