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9. ABSTRACT

Proceedings of a seminar/workshop on Pesticide Management held in Manila on February 10, 1975. Contains 12 papers presented by participants. The objective of this volume is to provide a background in pesticide management. The papers deal with such subjects as the use of pesticides in increasing food production, better protection of human health from vector-borne disease, prevention of human poisoning, prevention of environmental pollution, and avoidance of prest resistance. The papers are of interest to professional workers in agriculture and health, to administrators in those fields, and administrators in the chemical pesticide industry. Others who should find the papers of use are persons responsible for planning programs in developing countries. The purpose of the workshop sessions is to develop interdisciplinary teams to address the problem of developing pesticide management teams, a clearinghouse to deal with problems of persistence, resistance, and poisoning, and a capability for monitoring and analyzing pesticide residues. These teams will also make recommendations for implementing these pesticide management problems.

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THE AGROMEDICAL APPROACH TO PESTICIDE MANAGEMENT

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Opening ceremonies (Manila, the Philippines, February 10, 1975) of the third in a series of Seminar/Workshops on the subject of Pesticide Management. This series is sponsored by the United States Agency for International Development and the UC/AID Pest Management and Related Environmental Protection Project for the purpose of assisting countries improve their pesticide management practices. These Seminar/Workshops are presented in cooperation with local, national and international agencies of the participating country as well as private industry.

PREFACE

The objective of this volume is to give a background on pesticide management aimed at: a) assisting in increasing food production; b) better protection of human health from vector born disease; c) prevention of human poisoning; d) prevention of environmental pollution; and e) avoidance of pest resistance. We hope that professional workers in agriculture and health, and administrators in those fields as well as the chemical pesticide industry will find it of interest. Others that should find the manual of use are those responsible for planning programs of the country and of industry. The volume is based on presentations offered at previous Pesticide Management Seminar/Workshops sponsored by the UC/AID Pest Management Project. Additional copies may be obtained from

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INTRODUCTION

Ray F. Smith

Director

University of California/AID Project in Pest Management

On behalf of the University of California/U.S. Agency for International Development Project in Pest Management and Related Environmental Protection, I would like to welcome you to this seminar/workshop on pesticide management. This meeting offers an exceptional opportunity for us to come together and focus our attention on the mutual problems facing us with regard to pesticide use in the agriculture and public health sectors of our communities. The purpose of this seminar/workshop is to provide you with a greater knowledge and understanding of pesticides and also to acquaint you with the technology known as pesticide management.

Briefly stated, pesticide management is the technology concerned with the safe, efficient and economic use and handling of pesticides from the time of manufacture until final utilization and disposal. Included in this process are formulation, packaging, transport, storage, official registration for use and sale, selection for use, application, and the disposal of containers and unwanted material. In addition, pesticide management is concerned with the problems of residues in food and the environment and their impact on the welfare of man. Without question, pesticide management must be considered an integral component of sound pest and vector management.

It is appropriate at this point to ask: How can the safe handling and use of pesticides be achieved? Ideally, pesticide management is achieved through a multidisciplinary attack known as the agro-medical team approach. This approach combines the many talents and expertise of the medical and agricultural sciences in attacking the pesticide management problems common to agriculture, health and society, and has already been utilized in a number of countries. The logic of this agro-medical team approach has been demonstrated in these countries and stems from the fact that the well-being of a community is found not only in its economic status, but in its nutritional and health status as well. Sound pesticide management can make a considerable difference to the economic, nutritional, and health status of a village, city, country or region.

The need for training in pesticide management has existed for many years, but only within the last few years has the vital importance and urgency for providing this training been widely recognized. The signs are unmistakable that we live in one of the most critical periods of man's existence on earth. The next few years must provide answers to

most vital questions for man and his well being. Can we produce an adequate food supply for the world's population? Can we do this without irretrievably destroying our environment and its future productive capacity? Can we control or eliminate the diseases of man that continue to erode his health and well-being?

A critical element in a satisfactory and complete answer to these three questions is pest and disease control. We cannot produce an adequate supply of food without improved pest control. We cannot maintain the quality of our environment without a more ecologically oriented pest control. We cannot control many of the diseases which plague man without good pest control.

It is for these reasons that plant protection and pest control are placed in a new context today as compared to that prevailing as short a time ago as five years. The world's expanding human population requires an increasing supply of food and fiber. To obtain this larger supply, better protection will be required from diseases, insects, and other pests. Unfortunately, the task of achieving this desired goal of improved production through better pest control has now become more difficult. There have been great increases in food production in some regions of the world. These increases have been achieved through use of improved varieties, cultural methods and to some extent pest control. However, the protection of this new food supply rests on a very shaky foundation. For example, we have narrowed the genetic base of our agricultural crops and the ability of these crops to resist new pests or old pests in new form. The resistance in certain insect populations has greatly reduced the effectiveness of chemical pesticides in a number of important situations.

Nevertheless, despite a variety of very difficult problems associated with our chemical pesticide, e.g. human intoxication, destruction of beneficial insects, and development of resistance, these pesticides still are essential in the protection of our crops and our health. In fact, the pesticide shortages which have plagued us recently have dramatically demonstrated the essential role of pesticides.

This Seminar/Workshop is planned as a study/work session to provide a functional plan for improved management of pesticides in this region. The presentation of technical talks on such topics as pesticide chemistry and metabolism, biochemical and physiological effects of pesticides, medical aspects of pesticide poisoning, pesticide formulation and application, agro-medical approaches to pesticide management, etc., is for the purpose of sharing a common knowledge base with you with regard to pesticides, their properties, use and toxicology, and the problems of persistence, resistance and poisoning in relation to pest management. The workshop sessions have as their objective the formation of interdisciplinary teams which will address the problem of developing a system and organization for the establishment of pesticide management teams, a clearing house activity to deal with problems of persistence, resistance, and poisoning, and a capability for monitoring and analyzing pesticide residues. These teams will also make recommendations for the implementation of these pesticide management programs. We look forward to improved pest control resulting from the recommendations of this meeting and thus increased crop production and improved human health.

We, who are representatives of the UC/AID Project in Pest Management and Related Environmental Protection, are most pleased to be able to work with you in this Seminar/Workshop. We look forward to an extremely productive session.

'GROMEDICAL APPROACHES TO PESTICIDE MANAGEMENT

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History and Assessment of the Problem

The combined effects of increased population growth and the simultaneous need to produce enough food for the world is one of the most urgent and challenging problems that faces the governments of the world today. The problem is of equal concern for the developing and developed countries - in fact it is a global problem.

While concerted attempts are being made in many areas of the world to try and find solutions to the problems of this expanded growth, it does not appear that the solution is presently at hand. Demographers forecast a doubling of the world's population by the turn of this century so that efforts to avert starvation and famine must proceed with utmost vigor.

Many countries are evaluating the situation, seeking to ascertain whether present efforts and programmes are sufficient to meet the demand. For example, the University of California/USAID Project which represents a broad approach to global pest management, utilizing the multidisciplinary skills from several universities of the United States, is supported by the USAID program of the State Department. This project has already conducted seven multidisciplinary pest management studies in different parts of the world. In addition to pest management, pesticide management has received special emphasis. And in furtherance of this goal, pesticide management seminars involving agriculture and health have been conducted in El Salvador, Indonesia and in the Philippines where the problems of pesticide management were explored and approached by both disciplines.

It is apparent from these seminars held in different areas of the world that neither discipline questions the continued major role that pesticides must play in the future needs for increased food production and the continued control of human vector born diseases. Pesticide management is seen as an integral component of pest and vector management; it is our belief that the ultimate goals of improved food production and the control

of vector born diseases will only be achieved through the integrated approaches to pest management, a philosophy which Dr. Ray Smith is one of the leading advocates of in the world. Safe pesticide management is therefore an essential component and possibly a prerequisite of integrated pest control.

During our interdisciplinary involvements in the pesticide management seminars in these several areas of the world, three problems of pesticide management were recognized. These were:

1. The growing problem of human poisonings;

2. The problem of persistence and the pollution of food and man by trace amounts of pesticide residues in the environment; and

3. The growing problem of increased pest and vector resistance.

These were problems which were of equal concern to the disciplines of agriculture and health. The common interest of these three problems to both disciplines prompted us to coin the phrase "agro-medical" problems of pesticide management. Not only were the problems of mutual interest to agriculture and health but so also was the solution thereof. Since our first recognition of these three problems in El Salvador, world political events have produced a fourth problem, namely, the problem of pesticide shortages and the need in the future for pesticide conservation. This topic is discussed in another presentation in this report. In this presentation, evidence is provided which emphasizes the reality of the pesticide shortage and demonstrates the need for pesticide conservation and the furtherance of integrated pest control approaches. I would like to provide you with some data which, I believe, is supportive of the seriousness of the other three problems - namely, poisoning, persistence and resistance.

Human Pesticide Poisonings

This topic has been more than amply covered in the different seminars, and there are copies of these early reports available. Many of these reports qualify the data by stating that accurate measures of poisoning incidence are incomplete. Pesticide related illness and poisoning are not reportable in most areas of the world and for the most part are seldom investigated thoroughly. Seldom is there information given which describes the type and nature of the exposure, clinical findings, the result of agricultural investigation of the causes of the poisoning and the appropriate back-up of chemical and toxicological investigations. Nevertheless, the statistics, such as they are, are impressive. As has been mentioned, the WHO estimates there are 500,000 pesticide poisonings occurring annually, and there is probably a 1% mortality rate. During our visit to El Salvador, there was reason to believe that accurate statistics of human pesticide poisoning were being collected, and these have been listed in Table 2 in the presentation of the "Current Medical Problems of Pesticide Management," included in these proceedings. Similar data, although still sketchy, were

collected during a survey of Java, Bali and North Sumatra by the author in 1967-68. Information was obtained on 478 cases. Following this, pesticide protection teams were set up in Indonesia in 14 provinces, and in contrast to the earlier survey, 452 poisonings were reported. On this occasion, the organophosphates were the major chemical compounds involved, and 138 OP poisonings were reported whereas in the earlier survey, the organochlorine pesticides were the major offenders. The concept of pesticide protection or management teams utilizing an interdisciplinary approach to the problem was pioneered by the Ministry of Health in the government of Indonesia. At present these pesticide protection teams consist of a public health officer, who is usually a physician with special expertise in this area, and a chemist or a pharmacist. The latter has received special training in cholinesterase testing and thin layer chromatography. Cholinesterase measurements are obtained by tintometric studies, and the WHO has provided the necessary equipment to these 14 provinces.

The Problem of Persistence

The problem of accidental contamination of food, particularly meat and tobacco, has been encountered in several areas of the world. Central America, too, has had problems of residues on meat on occasions. This once temporarily prevented the export of beef because organochlorine residues exceeded the acceptable tolerances of an importing country. These accidental conatminations led to economic losses in the exporting countries and raised questions as to how best dispose of the contaminated products. Of equal concern in the health field is the magnitude of human contamination. While no adverse human health effects have heretofore been demonstrated from the ingestion of these small traces of pesticides, the chemical profile of our environment is changing rapidly, and few will question the need for regular human monitoring programs for trace amounts of pesticide chemicals, non-pesticide chemicals, contaminants and other environmental pollutants which can be measured in the fat, urine, hair or other appropriate tissues of the human body. The need for descriptive epidemiologic study of the frequency distribution of these environmental pollutants in the general population has been stressed and the representativeness of the sample emphasized, especially with regards to sample size and the amount of stratification required for demographic and geographical variation.

Problem of Resistance

This is the third pesticide management problem encountered by the Project. The present status of pest resistance in insects in different areas of the world is of interest to crop protection experts. Likewise, the problem of anapholine resistance is the concern of public health. This was especially seen in Central America. Here in the past, the successful vector control program for malaria has achieved the goal through the application of DDT within the home - a locale which does not significantly contribute to the contamination of environment by this insecticide. However, several authorities have

argued that the agricultural uses of pesticides have afforded the malarial vector the opportunity to acquire resistance. This certainly seemed to be the case in Central America where malarial control programs relied firstly on DDT, then later on dieldrin and finally on propoxur to achieve control. At present in El Salvador and in Guatemala, Anopheles albimanus, the local vector of malaria, is resistant to all three insecticides, and Georghiou has suggested that the agricultural use of parathion on cotton has facilitated the development of a cross resistance of this mosquito to propoxur. The epidemiologic data certainly support this concept, and there are two coastal areas in El Salvador and two similar areas in Guatemala where the reports of vector resistance to propoxur coincide geographically with areas where human parathion poisoning is most frequent.

These several problems are clearly of concern to both agriculture and health, and it is this mutual interest which has prompted us to propose this "agro-medical approach."

Concepts and Accomplishments

Certain fundamental concepts underly the agromedical approach to pesticide management. Some of these may sound unworkably idealistic calling as they do for human beings to rise above their parochial interests to work together toward the goal of the common good. But there is an urgency brought on by current conditions that demands such a response on our part. It is our conviction that in rising to the challenge we do not suffer sacrifice but rather all gain in physical and economic well-being.

The first concept or premise is that the problems of physical (health) and economic well-being of the rural areas are inextricably interrelated so far as man is concerned. Without food and money, the most beautiful of environments appears to man to be but desolation. In like manner, neither can riches compensate for loss of health. Thus, the concept of agromedicine embodies a "holistic" approach to community well-being involving food production and protection of health of both man and his environment. We are, of course, considering here the rural areas.

Deriving from this concept is the premise that achievement of the implied goals calls for a coordinated interdisciplinary approach. In the beginning certain primary disciplines must lead the way. The smallest such group is that made up of the agriculturists (biologists), health practitioners and chemists. This comprises our base agromedical team. As we see it, in many countries the primary and sometimes most effective contact with rural people is the agricultural worker - either government extension or industry representative. In the agromedical approach, we believe this individual should be regarded as and given the responsibility for primary "community care" in the areas of food produ ion and preventive health practices. He does not supplant the public health practitioner nor the agricultural expert but serves as their entré in dealing with the problems.

It is easy to see this responsibility for the government worker, but how about the industry representative? Here we believe the interests of government (society) and industry converge. Consider the benefits (profits) that can and would accrue to industry from a healthy, productive and economically sound community in which resides a reservoir of good will toward the industry (company) that helps it.

Our "community worker" must be trained in pesticide management, agriculture and the practice of hygienic measures, and it is here where the agromedical team concept comes into play. These teams provide the necessary short term training in relevant fields and practices and the necessary support services, such as analytical chemistry, field investigations and health care delivery.

The next element is that of the agromedical teams, beginning with the district or region and continuing to the national level. At each level the breadth of expertise and capabilities to provide service and do research increases. Conjoined at the different levels are the various government agencies for research, regulation, universities and extension, and as full working partners the complex of related industries as a Coordinating Council. This may be accomplished by the formation of a supra-team of representatives of each group with resources of expertise to provide suggestions on needed regulations, research, training and technical assistance. But more, this group can invoke cooperation and assistance at the international level.

Very well and good, you say, but has it been tried and does it work? This is a valid question, and perhaps the best response is to be seen in the several seminar-workshops. In them we have seen, often for the first time, agriculture, health, food and drug, pollution control and other agencies meeting together to discuss and act on these problems. I am sure that more action and interaction has continued to follow.

We have seen the agromedical approach being applied in El Salvador and more recntly in Indonesia. From this action is coming wider dissemination and application of technical knowledge, upgrading of laboratory services and reduction in human poisoning and residues in crops and the environment.

The program is developing even more dramatic results through research such as improved formulations - safer and more effective, protective clothing adapted to the climate and economics of the tropics. It is resulting in better human and environmental monitoring, increased productivity and, we believe, profits for agriculture and industry. Above all, it is improving communication and teaching us how to work in a coordinated interdisciplinary manner on the complex problems that beset us. Yes, the concepts may be idealistic, but in our opinion, the results to date have been both pragmatic and profitable.

Suggestions for Use of Pesticide Management

My colleagues of this agromedical team have described a wide-ranging multi-faceted philosophy or approach to the very large problem

of pesticide management. In fact, the real or total problem is much greater than pesticide management because pesticide management is only of significance in terms of pest management (i.e., pest control for health or agriculture). Pest management, in turn, is only relevant in terms of increased food production and improved health of man. This total aspect is indeed a very large and very complicated problem. It is a problem that is not susceptible to simplistic or unilateral approaches. It must be approached systematically in a holistic manner (i.e., with consideration of the entire problem, not just the parts). In the modern vernacular this is the "systems approach"; in terms of pest control, it is the "integrated pest control" approach; and in terms of pesticide management, it is the "agromedical team approach."

To be more specific, what does this mean in terms of the seminar-workshop on pesticide management? In the first place, the workshop groups have the task of defining the future plan for activities in pesticide management. This proposed plan should provide for both the short term and long term aspects of pesticide management. In this connection I would suggest that consideration be given to an "Interagency Coordinating Council" to maintain needed effective contact between the concerned groups, interchange of information and sharing of responsibilities. There are many reasons why such an Interagency Coordinating Council is needed. This may not be the appropriate title for a supra-agency coordinating body; the workshop should consider this point, the composition of the group and its functioning. The sheer size and complexity of the total problem associated with pesticide management will be more than the available resources of this country or almost any country can handle. This means that resources should not be wasted through duplicative or misdirected efforts; the available resources should be directed through coordinated efforts to attack, at least at first, only the most important priority areas. An Interagency Coordinating Council is sugggested as an effective and efficient means of achieving this important objective of establishing priorities and responsibilities for them. As an aside, I wish to point out that the problem is so large that no one should feel left out or put down by this proposal. There is plenty of room for all to work at their fullest capability.

Future activities in the pesticide management area should be many and varied (but hopefully well coordinated under the Interagency Coordinating Council). One large area will involve monitoring, regulation, legislation and enforcement. Many of these topics, at least in their short run aspects, will be carefully reviewed by the workshop groups. I wish only to stress here the importance again of the coordination of the activities of the several agencies in this "administrative area" and the importance of looking forward toward the gradual evolution and improvement of monitoring, safety and enforcement. A piece of legislation or an agency regulation is not an end in itself. It only has meaning if its application results in improvement of man's total environment or advancement of the common good of society. Progress in this direction will require continual evaluation of the state of pesticide management.

The improvement of pesticide management will also require developments in research and training. A number of needed research areas have been mentioned in the earlier presentations of the seminar-workshop, e.g., pesticide formulations to suit pest and environmental conditions of each country, protective clothing suited to the tropics for workers exposed to pesticides. The large research area of integrated pest control involving, for example, establishment of economic injury levels, evaluation and utilization of natural enemies, and incorporation of cultural controls and resistant varieties, is also of immense importance in the total pesticide management picture.

The need for education and training has been stated many times during the course of the various seminar-workshops. Again these activities should be coordinated among the agencies and clear priorities established. Of high importance is education of the general public - both urban and rural - to the values and risks of pesticide usage. There is also a need for general public knowledge of the objectives and methods of the country's pesticide management program. Again, I leave it to the local agencies to design the details of this program of public education. The level of technological expertise at all levels should also be continually upgraded. Overseas training is only one of the many means available for this type of training. On the job training and regular periodic workshop sessions should be established for personnel in the several agencies working with the same or similar technical aspects, e.g., gas chromatography, diagnosis of pesticide poisonings. Finally, I would suggest that perhaps it would be most profitable for the members of the seminar-workshop to come together again to discuss progress in pesticide management along these lines in 12 to 18 months.

In addition, there is a great value for pesticide management to have coordination of activities and information exchange on both a global and regional basis. WHO and FAO are initiating some activity along these lines, but strong support for the regional and global program should also come from this country (region).

A number of residue laboratories have now been established recently around the world. Although these laboratories may have different primary objectives and responsibilities, they in fact are utilizing the same kind of equipment to make similar analyses. This large number of laboratories is of itself a problem and some procedures must be established for effective quality control among them. This is essential for comparison of data originating in different laboratories. Again, suggestions for details of the procedures to be invoked should come from the workshop groups.

Finally, I would like to say something about the common interests and mutual responsibilities of agriculture and health in the pesticide management field. In this important area, health and agriculture must work together because neither can handle the problem adequately alone. Health agencies are concerned primarily with the health and well-being of man, but they also recognize their requirement for pesticides to control medical pests and vectors of disease. Agriculture agencies utilize pesticides to increase the supply of food, but they also recognize the importance of the quality of man's health in maintaining an effective work force. Man does not live by food alone. A supply of rice is not enough. The well-

being of the rural community is inseparable from its health status and its economic status. The missions of health and agriculture coincide in the "well-being" (in every sense of the term) of the rural community. Agriculture, health and the other important members of the team should work together to achieve that "well-being."

The UC/USAID Pest Management Project stands ready to assist you in the improvement of pesticide management in any way that we can - not only in this seminar-workshop but in the future. Please call on us.

WORLD PROBLEMS OF PESTICIDES

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Introduction

The trends and extent of growth for the production and use of pesticides since World War II are reasonably well documented for the industrial countries of North America, Western Europe and Japan. The overall amount of pesticides sold to the developing countries as a group is also reasonably reliable, but the figures for individual countries and even more, the uses made of these imported pesticides are not readily and reliably available.

Nearly all pesticide production is limited at least in large part to the industrialized countries of Europe, North America and Japan. Although much of the parent pesticidal compounds are formulated in final commercial form in the developing countries, and in less frequent cases some steps in the synthesis of the parent compound may be carried out in the developing country, nevertheless, there is very little production that includes all steps of synthesis and final formulation.

Although the rate of growth in pesticides use in developing countries has tended to be higher in recent years than in the developed countries, the small base from which this growth started still results in the total tonnage of use by all developing countries being small in comparison with the countries with highly developed modern agriculture. In 1970, the United States consumed 45% of all pesticide production, Western Europe 23%, Eastern Europe 13%, Japan 8% and the developing countries 7%, with the remainder in Australia and other developed countries.

The relative growth rate between insecticides and other pesticides has been much less in the developed world compared with the developing world. In the developed world, insecticides have declined in relative position among pesticides from being the dominant class of pesticide before 1960 to representing only about one-third of total pesticide usage currently. This is in spite of large increases in total tonnage of insecticides used. This is primarily the result of the rapid

growth in the use of herbicides which now represent the major portion of pesticides used on a global basis and are still increasing in use at a more rapid rate than other classes of pesticides. There is strong indication that this trend may accelerate as farmers are increasingly substituting herbicides for tillage because of higher fuel and equipment costs and equipment shortages. In the developing world, insecticides remain the dominant class of pesticides used, and their use is increasing at a rate that would appear to maintain their dominant position for some time to come.

The use pattern by crops for insecticides is fairly well known for the United States and some of the other developed countries, but it is not well documented for the developing countries. In the United States about half of all insecticide usage in agriculture is in cotton. Maize represents about 10% of all use; and of the fruit crops, apple is one of the major consumers. In developing countries, it is hard to evaluate end use of imported pesticides because they are used extensively in public health programs in addition to agricultural uses; reliable figures on relative uses by sector and specific crop are not available. Nevertheless, it is clear that in the past, nearly all agricultural use of pesticides in developing countries has been on cash crops, with cotton representing at least half of all use. Plantation crops such as sugarcane and tree crops have been major consumers of pesticides with vegetables, rice and maize, when they are raised as cash crops, of lesser but increasing importance. In some developing countries, use of insecticides to protect stored products is also of importance.

Current International Trends Affecting Agricultural Development

The disappearance of basic food stock reserves has led to a rapid increase in prices for basic food commodities. Some of these crops receiving high prices have often been marginal in pesticides use in the past, but now with their increased value there is a favorable cost/benefit ratio. Some plantation crops have also been affected similarly. These more favorable prices for the farmer should stimulate both production and demand for inputs such as fertilizer and pesticides. The impact can already be seen in shortages and rapidly escalating prices for these products. This, in turn, may well lead to greater emphasis by developing countries on increased local manufacture of pesticides, at least to the extent possible.

General inflation has become a worldwide problem. It is seriously affecting the balance of payment position of both industrial countries and those developing countries which are not major exporters of raw materials. The balance of payment problems are expected to increase the desire of agricultural product exporting nations to increase their production as a means of easing payment problems, and for the countries who are net importers of agricultural products to expand local production of agricultural products to reduce import requirements. Since both of these current trends could increase pesticide demand substantially, they could have a major impact on the pesticides industry. This is particularly true because pesticides

usually produce a high rate of return on money invested by the farmer. The rate of return can be greatest in developing countries where low base productivity permits greater cost-benefit potential.

The rapid price rise in petroleum products has heavily affected the pesticide industry. Most pesticide manufacture involves petrochemical products either as basic building blocks in manufacture or as solvents or emulsifiers in formulation. In addition, price increases for plastics, metals and paper products used in packaging are also affecting pesticide price. There are also periodic shortages of various pesticides which have added to the problems of users in developing countries.

Current Trends in Pest Control and Pesticide Usage and their Implications

The growing concern for greater protection of the environment, especially in developed countries, has had major impact on pest control programs. This is most strongly manifested in the efforts that have been made to restrict or eliminate the use of pesticides that persist in the environment over long periods. This is having a major impact on the use of chlorinated hydrocarbon insecticides.

The effort to restrict chlorinated hydrocarbons in developed countries has been taken up rapidly by most developing countries. This has had a major impact on both the availability and type of compounds used. This affects the cost of plant protection and other pest control because most of the alternatives prove to be much more costly.

Some of the adverse consequences of wide scale use of pesticides have caused some to advocate the elimination of most or even all pesticides. This is foolish because knowledgeable plant protection experts have been unanimous in recognizing that pesticides are essential for agriculture and public health for the present and the future. Nevertheless, certain adverse consequences of pesticides, e.g., development of resistance to pesticides, persistence of residues in food, destruction of beneficial organisms, and human intoxication has led to restudy of pesticide use patterns. This trend has produced interest in expanding the integrated control approach to crop protection. In this approach, primary reliance is placed on naturally occurring mortality with supplemental manipulation of parasites, predators and pathogens, on resistant crop varieties, on pesticides and on cultural practices to keep pests below the levels that cause economic damage. Pesticides are used in compatible ways and are kept to the needed minimum to supplement the other controls.

The expanded interest in integrated pest control has also created the demand for more narrowly specific pesticides which have greatest possible impact on the target pest organisms while at the same time causing minimum effect on other species in the environment. This has led not only to greater interest in developing highly specific pesticides but also in isolating natural compounds which can be used to manipulate pest populations. These include such chemicals as

hormones or hormone mimics that can disturb the normal development pattern and pheromones that can be used as attractants or whose use can confuse normal behavior. This same trend has caused increased interest in artificial rearing of parasites, predators and pathogens and in the genetic manipulation of pest populations.

Although these new trends will result in the development of new compounds, the continued use of older pesticide compounds will be necessary. Furthermore, these trends are fraught with many problems when it comes to maintaining adequate pest control capability for economical crop protection and production in the future.

Problems in the Development of New Insecticides, particularly specialty compounds and novel chemicals useful in pest control

One of the biggest factors which creates difficulty in the development of any new pesticides is the rapidly increasing research and development cost required to bring a new product to the market stage. This cost has reached the level of more than ten million dollars to get a new product on the market and requires an average of ten years to fulfill all the regulatory and performance requirements. Much of this large cost results from the greatly increased regulatory requirements that have generated from a heightened desire to safeguard man and the environment. These requirements are often only for the public interest and are beyond the requirements needed to insure an adequate agricultural market at reasonably assured levels of safety.

It is clear that we will be faced with increased pesticide prices and periodic shortages for the next few years. What can we do? We must conserve our supply of pesticides like a man in the middle of a desert conserves his one canteen of water. Pesticides must not be wasted. The insurance treatment applied because pests might be present or might do damage is wasted pesticide and the cost has become too high. To conserve pesticides and money, they must be applied at the correct dosage in the most effective manner possible and only when necessary. Where possible, the integrated control approach should be utilized because it makes maximum use of the naturally occurring mortality and thus extends the effectiveness of the available pesticides.

INTEGRATED PEST CONTROL AND ITS PRACTICAL IMPLEMENTATION

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Integrated control is a broad ecological approach to pest control utilizing a variety of control technologies compatibly in a single pest management system. In integrated control, stress is placed on the importance of realistic economic injury levels which are used to determine the need for control actions. At the same time, all possible is done to protect and preserve naturally occurring biotic mortality agents such as parasites, predators and pathogens. When artificial controls are needed, for example, chemical pesticide applications, they are employed in as selective a manner as possible and only when their use is economically and ecologically justified. The ultimate objective of the integrated control system is to produce the optimum crop yield of high quality at minimum cost, taking into consideration the ecological and sociological constraints in that particular agroecosystem and the long-term preservation of the environment. This is the ideal of integrated control toward which we work.

In view of the considerable discussion in many places about the term "integrated control," it is appropriate to describe what integrated control is not. It is not sole reliance on predators or parasites, although natural enemies are utilized and fostered as much as possible in the system. It is not classical biological control, although this technology is brought into use where possible. It is not the use of the sterile insect release method, nor is it the use of pheromones, hormones and other largely untested and unproven biological methods of control, although eventually we may be able to use such techniques in integrated control and are striving to do so. It is not the elimination or banning of DDT or any other chemical pesticide, although in a particular integrated control system it may be necessary to restrict the use of most pesticides and not use others. It is not the development over a long period, with much research effort, of a completely new pest control system which then is established in place of the old system; rather, the process is a series of incremental steps which gradually modify the old pest control system.

Today, most people involved with pest control define the term "integrated control" quite broadly. As an example, I would like to quote the complex one proposed by the FAO Panel of Experts on Integrated Pest Control. They defined integrated control as "a pest management system that in the context of the associated environment and the population dynamics of the pest species, utilizes all suitable techniques and methods in as compatible a manner as possible and

maintains the pest populations at levels below those causing economic injury." In its restrictive sense, integrated control refers to the management of a single pest species on a specific crop or in a particular place. In a more general sense, it applies to the coordinated management of all pest populations in the total agricultural or forest environmnet. Furthermore, it should be emphasized that integrated control is not simply the juxtaposition or superimposition of two control techniques, such as chemical and biological controls, but rather it is the integration of all suitable management techniques with the natural regulating and limiting elements of the environment. Integrated control derives its uniqueness of approach from its emphasis on the fullest practical utilization of the existing mortality and suppressive factors of the agroecosystem.

Principles: It follows from this discussion of the basic definition that integrated control has two fundamental principles to guide it:

The first principle is "consider the agroecosystem." In other words, pest control should be developed and applied in the context of the total environment. Pest populations are managed in such a manner that existing limiting and regulatory factors are exploited to the fullest extent possible and without disturbance to the regulation of other pests. This principle defines the underlying philosophical approach to integrated control.

The second principle is "utilize economic injury levels." The determination of levels of tolerable pest damage in agricultural crop lands and in forests is an essential prerequisite to the development of integrated pest control programs. Additional mortality or regulatory factors are introduced into the environment by man at appropriate times to maintain the pest populations at levels below those causing economic injury. These economic levels should be determined both in terms of the anticipated crop loss in the absence of control action and the economics of crop production and marketing. This principle defines the goal of the integrated control system.

Agroecosystems: The term agroecosystem is derived from the well-known ecological term "ecosystem" and emphasizes the special characteristics of agricultural ecosystems. The agroecosystem is a unit composed of the total complex of organisms in a crop area together with the overall conditioning environment and as further modified by the various agricultural, industrial, recreational and social activities of man. Note that the concept of "pest" is not an essential part of the definition of agroecosystem. In the practical analysis of the agroecosystem for pest management, we must center on the numbers of the pest species, their competitors, the organisms that prey on the pest, the main and alternative food supplies of the pest and the manner in which the other elements of the environment modify them. The determination of insect numbers is broadly under the influence of the agroecosystem and a knowledge of how this influence operates is essential to integrated pest population management. A thorough understanding of the agroecosystem is also necessary to harmonize the control practices for different pests in such a manner as to prevent unacceptable disruptive effects. In the same way, a knowledge of the agroecosystem permits assessment of the mortality factors

operating on a pest or potential pest population and will suggest subsequent manipulations to reinforce and enhance their action.

Man has been a dynamic element in his environment ever since his arrival on the scene, just as have other abundant species. His hunting, his use of fire, his agricultural practices (especially irrigation and overgrazing), his cutting of forests, and other unintentional acts have modified the landscape to a great degree. We have only to look about us in nearly any part of the world to see an example of how man has greatly modified the agroecosystem. The impact of man has so changed the environment in many areas that it is hard to find evidence of the original ecosystem that existed many centuries ago. Through his agricultural use of the land and through other activities, he has reduced complexity of the local environment and in other ways modified it. For this reason, it is useful to talk about this new man-modified ecosystem as an agroecosystem. The impact of man on his environment throughout the world is today steadily increasing and more than ever we must know what we are about. It is essential that we know enough about these agroecosystems to plan their management and their evolution.

Crop protection procedures are an important phase of the management of an agroecosystem. In the past, man through trial and error adapted his agriculture and other activities to the changes as they occurred. But now the pace of change is so rapid and our need for food production so great that there is not time for trial and error. We must have prior knowledge on which to base our control of the agroecosystem.

The concept of the agroecosystem applies to subsistence agriculture as well as to the most sophisticated of scientific agricultures. The point is that both are ecological situations, and to control or manage any ecological situation, you must use ecological principles. In our concept of the agroecosystem for integrated control, it is often important that we consider the pest species and their natural enemies as they occur outside of the specific crop area, e.g., on alternate hosts and in uncultivated areas.

Agroecosystems vary widely in their stability, complexity and size. It is also important to realize that they are in a continual process of evolution. Changes in cultural practices, crop variety or pest control procedures can greatly modify ecosystems. The limits are often difficult to define precisely, particularly with complicated environments and where pest species are involved that migrate widely.

The integrated control specialist - the pest manager - has to manipulate the agroecosystem. He relies for his decision upon an analysis of the biological and economic systems of pest control and crop protection which embraces all significant factors acting on the complex of real and potential pests and the interactions of such factors among themselves and with other processes in crop production. The integrated control strategy employs the idea of maximizing natural control forces and utilizing any other tactics with a minimum of disturbance and only when losses justifying action are

threatened. Insecticides must be used in agroecosystems; their targets are insects, but we must understand them in the context of agroecosystem. This is what integrated pest control attempts to do.

The importance of economic levels: Although economic injury levels have long been considered of importance in determining the needs for pest control, they take on added significance in integrated pest control. To clarify the fundamental relationships between insects and crop losses, it is convenient to make a clear distinction among the presence of insect numbers, what these insects do to the crop plants, and a subsequent loss of yield and quality in the harvested crop. The interaction of insect numbers and environment produces a behavior pattern that may or may not injure the crop plant, that is, result in plant damage. The plant damage may or may not result in crop loss, and in some instances, the damage to the plants may even be beneficial, and the result is an increased crop.

Crop loss is a reduction in either quantity or quality of the harvested product. Loss in quality may be in appearance, nutritive value or other values influencing the ultimate use of the crop. Any particular crop loss may or may not be an economic loss. From the broad view of human society, all crop losses must be considered losses. However, the farmer, the producer of the crop, considers only a portion of the reduction in yield or quality as an economic loss. His determination made consciously or intuitively, on good or bad advice, or however, will be influenced by such elements as the available technology for crop protection, cost of avoiding the potential loss, marketing conditions and the ultimate use of the crop.

Almost any aspect of an agroecosystem can have some significant influence on the pest complex and hence on plant damage and possibly on crop loss. This makes the assessment and evaluation of pest injury to plants and the establishment of economic injury levels very difficult. What are some of the factors involved?

Population density: The relationship between pest numbers and plant damage is rarely, if ever, a simple straight line direct function. Some levels of pest numbers and consequent plant damage have no measurable effect on crop yield. Other levels may have a beneficial effect in spite of, or even because of, significant injury to the plant.

The impact of insect numbers on plants is to a large degree conditioned by the time of attack. The plant may be able to compensate for damage from small numbers over a long period of time but not for an equivalent amount of damage delivered in a short period of time. In other cases, persistent low populations may accumulate harmful effects. Another aspect that makes it difficult to relate insect numbers directly to plant damage is the fact that pest populations vary greatly not only in numbers but also in quality. The composition of the pest population may vary with respect to the proportions of various stages, age classes, sexes and other characteristics. Obviously, this greatly influences the damage potential of the population.

Other elements involved in the establishment of economic injury levels are the dispersion of pests over the cropping area, difference in behavior of the pests, the condition of the plant, the ability of the plant to compensate for pest attack, carrying capacity for fruit by the plants, stage of development of the plant, cultural practices in the area and its physical environment.

What then is an economic injury level? It is a population density level of pests, a point below which the pest population and its consequent damage can be tolerated and above which it cannot be tolerated. Economic injury levels are best expressed in terms of crop loss, that is, reduction in yield and quality, and secondly, related to pest density as appropriate.

What is the special importance of economic injury levels to integrated control? The answer lies in the fact that in most crop protection situations we can tolerate significant population levels of pest species without economic damage. In some instances, these levels can be rather high, at least for certain periods in the cycle of crop development. The significance for integrated control is obvious. Subeconomic levels of the pest species must be maintained to support the entomophagous forms. These low pest densities serve as a food supply for a reservoir of beneficial forms that often will be needed later in the growth of the crop.

Much is left unsaid here about the complex ecological matrix known as economics of crop production. It, too, must be fully understood by crop protection specialists and fully meshed with ecology of pest species and their natural enemies. In many instances, crop protection decisions are made on a short term basis only. The complexities in the measurement of crop losses and the evaluation of pest-caused damage are many. We have only the beginnings of the information we will need to make sound interpretation of pest infestation and potential crop losses. Nevertheless, the difficulties involved and the size of the task should not drive us from the field. The values to be gained in proper evaluation of crop damage are great, not only for determining future research needs and agricultural plans but also to serve as a guide or goal for crop protection systems.

The integrated control specialist must be a field-oriented ecologist. He looks at all possible ways of manipulating the agro-ecosystem. What are his tools and his tactics? The main ones are:

1) Cultural control with its manipulations of plant dates, plant spacing, strip harvesting, interplants and trap crops.

2) Host plant resistance. It is especially important to remember that plant resistance need not be complete resistance to be useful in an integrated pest control program.

3) Use of parasites, predators, pathogens of the pests. This can involve introduction of new species, provision of shelter, supplemental food or alternate host and mass release

of artificially reared natural enemies.

4) Pesticides

These tactics are not used each in isolation but as a combined integrated system. Sometimes these are very sophisticated systems involving use of computers to handle large amounts of data and systems analysis methodology.

Now a few comments on some of the more important tactics of integrated pest control.

Microbial Controls: The horizons suggested for the introductions of new pathogens and the utilization of indigenous pathogens, particularly nuclear polyhedrosis viruses, have hardly been touched, even though the good results of milky spore bacterium of Japanese beetle in eastern USA and the polyhedrosis virus of the European sawfly in Canada are well known. Pathogens have many good properties as alternatives to chemical pesticides. It is likely that ones selective for certain species or groups of insects and innocuous to vertebrates abound in nature, but too little effort has been made to find them, characterize them and develop them for practical use. Pathogens have many of the advantages of chemical insecticides, and they lack many of their disadvantages. The pesticide application technology is adaptable to them. Some are quickly and highly effective, specific in activity, safe and biodegradable. In some cases, they can be readily stored. Their cost, lack of proved reliability, patentability and problems of registration clearance present some of the limitations. FAO and WHO are now making progress in establishing protocols for determining safety. The utilization of microbial controls, especially nuclear polyhedrosis viruses, has a very great potential in developing countries.

Natural enemies: Plant resistance has not developed to the point of accommodation or exclusion of all potentially destructive insects in respect to most of our common plants, and we cannot expect this in the foreseeable future. Rather, we find that most potentially damaging plant feeding species in natural habitats seem to be commonly held at low densities by their natural enemies. Except for special situations, extended control of the complex of pest species in agroecosystems is unlikely to be achieved unless natural enemies are made a primary consideration. Natural enemies have been a cornerstone in every developing or satisfactory program in integrated control. The host of pesticide-induced outbreaks reveals that many insects and mites in agroecosystems have effective natural enemies present. Much evidence suggests this "hidden" natural control that does not surface until we disturb the agroecosystem.

Employment of natural enemies has been in two principal ways: 1) introduction of new natural nnemies, usually from the native home region of the pest; and 2) manipulation of the environment of the host, and/or the natural enemies, such that that the resident natural enemies are made more effective. Even though only minimally researched and funded, introduction of new natural enemies has had far more success than has the manipulative approach. Introduction still presents

many untried possibilities. The introduction of highly selected genetic stocks is particularly promising. The manipulative approach (including use of pathogenic microorganisms and strategic releases of the natural enemy or the pest itself) has not been investigated extensively or with adequate ecological sophistication.

Plant resistance: Over the eons of time, plants have developed a multitude of mechanisms of resistance to insects and disease organisms. A vast pool of such resistance factors exist in plant stocks, and these germ plasms can be used in insect and disease control. Insect-resistant varieties provide an ideal way to control or suppress insect damage to crops. They involve minimum production costs, leave no insecticide residues in food or the environment, harm no pollinating or otherwise beneficial insects, only minimally disturb nature's balance between destructive insects and their natural enemies and are compatible with biological, chemical, cultural and other control methods.

Plant pathologists have used plant resistance extensively. Until recently, entomologists have made relatively little use of it in spite of some notable early successes. More recent work on alfalfa, cucurbits, wheat, rice, sorghum and corn has, however, been attempted with some success. Significant increases in effort must be made to develop acceptable cultigens resistant to a complex of pathogens, parasites and insect pests. The development of resistant varieties will probably not be available for whole complexes of pests, for a resistance factor for one pest may also be predisposed to attack by another. For example, there is evidence of a genetic linkage in lettuce between susceptibility to turnip mosaic virus and resistance to downy mildew. Moderately resistant germ plasm may have more place in an integrated control system than previously thought.

Cultural and physical control measures: The use of cultural practices in insect pest population has over the years provided significant contributions to crop protection and in some instances has provided good to excellent control. These measures have involved timing of planting and harvesting to minimize infestation or to escape periods of great danger, rotating crops (including varieties), manuring, managing water, crop residue destruction (e.g., burning), trap cropping, cultivation and barriers. Use of such methods in general interferes with the pest's development, e.g., commonly through exposure to rigors of environment and in fostering plant resistance or natural enemy action. Very often these cultural control practices can be improved by increased knowledge of the phenology of the pest and its host range, pest behavior, etc.

Cultural control may also involve more sophisticated techniques such as the selective use of preharvest chemicals, varietal modifications, pheromone manipulation of pest populations and the selective placement of insecticides. This tends to blend the traditional cultural controls with the new. Most often, cultural practices are used to achieve partial suppression of pest numbers in conjunction with other measures, especially chemical control. To be most effective,

cultural practices often have to be carried out on a community- or area-wide basis. In this way, they may be used to achieve population suppression of a pest over a relatively large geographic area.

Development of many new pesticides after World War II released growers from their reliance on these rather unspectacular cultural methods of pest control; subsequently, they have been much neglected. Cultural techniques do not commonly give complete control of a complex of pest species, yet they present real promise for use as supplementary tactics in integrated control, and they may form the principal means of control in certain situations.

In considering cultural and other methods of control, we must closely consider relationships with other agroecosystems, for faunal elements often move among several agroecosystems. The cultural practices, including modifications of the mosaic of crop or variety plantings affect the pest species, their parasites, predators and pathogens, or alternate prey or hosts. Adding habitat diversity may be helpful, e.g., small blackberry patches planted next to grape vineyards in California have shown the potential of achieving biological control of the grape leafhopper. Strip cropping of alfalfa and cotton has also been used to increase natural enemy effectiveness. A change from tillage to herbicides for weed control, from clean culture to a cover crop, or from selective age-distribution cutting to clear cutting in forests can have far-reaching effects on pest densities.

Much potential rests in the possibilities of rotation within a given field and in shifting the mosaics of plants in a region, particularly a group of varieties offering resistance to different species of insects and other pests.

Selective pesticides and selective use of conventional ones: While the prospect for obtaining registered products of high physiological selectivity looks to be unpromising at present, there are promising ways of obtaining ecological selectivity using conventional materials. Since insecticides remain our most reliable and practicable tool for immediate solution to many pest problems, we cannot afford to neglect the search for suitable selective materials and ways of selectively using conventional ones.

Fortunately, the development of effective and economical systems of pest management for the control of many major pest species is not dependent upon physiological selectivity provided by the availability of a large number of narrowly selective pesticidal chemicals. Pesticides having the broadest spectrum of activity may be used in an ecologically selective manner. As far as pest management is concerned, it appears that the selective use of insecticides (ecological selectivity) will continue to be far more important than use of selective insecticides (physiological selectivity). Selective action of non-selective chemicals can be obtained by manipulating doses, formulations, timing of applications, method of application and localization of area to be treated.

Other selective measures not yet broadly proved in practice include the use of sterility and genetic tools, and hormonal and behavioral chemicals. Insect hormonal chemicals, a variety of biochemical determinants of behavior, notably pheromonal type chemicals, and genetic interferences with reproduction (genetic tactics) have stirred imaginations of entomologists looking for a third horizon of insect control. The ingenious sterile insect release method (SIRM) has met with some striking field results. Some, however, think that inherent problems associated with the biologies of many insect species would preclude SIRM method from very general utility. Others are more optimistic as to the future impact of genetics in pest control. Genetics may also be used to enhance other systems of pest control, especially biological control, the development of biological insecticides and ways of extending the useful period of conventional insecticides.

Up to now, the behavioral biochemicals have been of practical use primarily in monitoring when used in conjunction with other methods as the actual control tactic. However, pheromones offer the possibility of being developed into a useful direct control tactic. Developments have not progressed far enough to establish their probable utility or possible adverse consequences.

Pheromones inducing an attractant response have been identified for many important pest species. Advances toward active pest control remain slow due to limited understanding of insect behavior as related to these chemicals, problems associated with isolation and identification of trace compounds in complex mixtures, or because of synergism and masking effects and difficulties in synthesis. There are also serious problems in developing control techniques that can utilize these compounds. There is now considerable evidence that none of these new technologies will be panaceas, and problems of resistance, residues and undesirable ecological side effects will also be associated with many of their applications. For the foreseeable future, these new technologies must be looked upon as potential weapons which will be added gradually to the crop protection scientist's arsenal. Furthermore, the systematic gathering of qualitative and quantitative information on pest ecology and behavior is essential if many of the newer, as well as the older, non-pesticidal control techniques are to find their proper place in systems of crop protection.

Finally, it is important also to develop methodology for implementing the pest control systems.

Implementation programs: For more than 25 years, a great variety of efforts have been made in the United States to take the results of integrated pest control research to the practical level in farmers' fields. In the forties, this involved a number of scouting and supervised control programs for alfalfa, tomatoes and cotton. In the mid-fifties, the spotted alfalfa aphid had its severe impact, and an integrated control program involving resistant varieties, parasites and predators and selective use of chemicals was devised and

implemented. In the sixties, research programs in integrated control expanded greatly on many crops. Many of the results of these studies carried over into the farmer's crop protection practices. However, there were very few organized efforts to establish large scale control projects based on integrated control. During the last four years, this has changed largely through a major cooperative effort of the several states and the federal government. During the 1972 growing season, there were about 40 such pilot programs involving 29 states. About one-third involved cotton; however, corn, grain sorghum, lettuce, apples, peanuts, tobacco, seed alfalfa, pears, peaches, peppers, potatoes, citrus and beans were also involved. These programs are partially supported by the federal government with the remainder of the costs paid for by the farmers.

These demonstration or pilot trials are still under development and review. In some cases, perhaps the pilot projects are too far ahead of the information developed by research. Ideally, there should be a close interplay between on-going research and the pilot project. There is a considerable "twilight zone" between research and implementation, and these demonstration trials provide a good mechanism for the necessary exchange. Some of the new pilot projects in integrated control now have a specific applied research project backing up the pilot demonstration trials.

Integrated control systems will not arise automatically from research emphasizing the new pest control techniques nor from long term basic research alone. The practical integrated control programs available today have arisen only from pragmatic research directed at finding solutions for the real crop protection problems as they exist in farmers' fields. In nearly all cases, integrated control programs have come about as the result of a gradual evolution in which new technology has been introduced in a step-by-step process rather than through the introduction of a complete fully-formed system.

In the early development and implementation of integrated control, emphasis was first placed on the importance of integration of biological and chemical control. Later, this was expanded to include all appropriate technologies. Now as we are attempting to develop ecologically sound crop protection systems for our agro-ecosystems, we must place equal emphasis on the integration of all the crop protection disciplines. The plant pathologist, nematologist, weed scientist and entomologist must coordinate their efforts with those of the economist, plant breeders, agricultural engineers and systems ecologists to produce ecologically sound and economically sound crop protection systems.

Although I have emphasized that only through the closest tie between the research and implementation efforts can either succeed and that they are both sterile without this interplay, it must also be stressed that implementation programs cannot move far ahead without parallel educational programs.

To improve the implementation of integrated control programs, an immediate broad educational approach must be made including training and retraining of crop protection and pest management specialists and the education of both farmers and the general public in the importance of crop protection matters.

Many active crop protection administrators, researchers, teachers and extension workers received their formal training during the fifties and early sixties when an over-reliance was placed on pesticide chemicals for crop protection. Now many of these crop protection personnal are becoming increasingly aware of the importance of a broad ecological approach to crop protection and the significance of an intensified attack on practical problems threatening food production. Their earlier training is inadequate to meet these new goals, and much additional training will be needed. A great variety of tactics are available to achieve these training objectives, including short courses, workshops, conferences, short-term consultants, and most importantly, active participation in collaborative research projects.

Substantial efforts should be made to inform the general public as to the severe food losses caused by pests and diseases and the significance of an ecological approach to crop protection and the preservation of environmental quality. An informed public is an essential step in the implementation of adequate and effective crop protection programs.

Many educational institutions are now in the process of reorganizing and revising their curricula in crop protection to provide a broad, ecologically-oriented training in integrated control and pest management. With the greatly expanded integrated control research and implementation programs, properly trained specialists are in short supply.

THE IMPLICATION OF AGRICULTURAL INSECTICIDES IN THE DEVELOPMENT OF RESISTANCE BY MOSQUITOES

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Abstract

Insecticide resistance in mosquitoes attributable to indirect selection pressure by agricultural insecticides is emerging as a serious obstacle to the successful control of vectors by residual house spraying. Evidence of the implication of agriculture insecticides consists of (1) correlations between the intensity of insecticide use on crops and the degree of resistance in mosquitoes, (2) seasonal fluctuations of mosquito resistance in parallel with periods of agricultural spraying, (3) correspondence between the spectrum of mosquito resistance and the types of insecticide applied to crops, and (4) suppression of mosquito population density in sprayed areas. Measures proposed for alleviating this problem are (1) collaboration between appropriate international agencies and governments for the purpose of identifying and reserving certain insecticides for use exclusively in public health, (2) introduction of comprehensive pest management practices in agriculture, and (3) greater emphasis on supplemental mosquito control measures.

Introduction

Insects affect not only the health of man but also his many crops, animals and stored products. It has been estimated by FAO that crop losses due to insect pests worldwide are about 12% of potential production.(1) Since insecticides constitute the most practical means of reducing these losses, they are being used extensively throughout the world. In 1972 the global insecticide production was estimated at approximately one million tons.(2) Despite current shortages, there is little doubt that the worldwide demand for pesticides will increase as developing countries strive to reap the benefits of new, high yielding varieties, in order to feed their increasing populations.

In the absence of strong economic or policy constraints, a five-fold increase in worldwide use of pesticides is projected by the year 2000.[1]

Strange as it may seem, intensive efforts to control pests of crops by insecticides have in a number of cases diminished man's ability to control mosquito vectors of human disease in the same environment. The ready availability of pesticides, often unaccompanied by adequate controls, has led to excesses in the frequency of their use and in the quantities applied. These abuses have not only complicated agricultural pest control by the selection of resistant strains of pests and suppression of biological controls, but have also altered, in some cases profoundly, the susceptibility levels of insect vectors of human diseases.

Insects of medical importance, especially mosquitoes, are often found breeding in agricultural habitats and are hence exposed to the insecticides employed in agriculture. This exposure may have a strong suppressive effect on mosquito density for some time, especially when the treatments affect the adult flying population.[3] However, the contamination of larval habitats also results in suppression of natural enemies of mosquitoes and, more importantly, in accelerated development of mosquito resistance to insecticides.

During the last few years, reports from various parts of the world indicate that mosquito control has become more difficult in areas of intensive agriculture due to decreased susceptibility of the mosquito.[4] It has also been observed that mosquito resistance of a level sufficient to impede their control has been most severe in areas where crops are treated frequently with insecticides. An increasing body of information points to a direct cause-effect relationship between the use of insecticides in agriculture and serious problems in mosquito control. This paper discusses some of the available evidence and proposes measures for coping with or alleviating this problem.

Reported Cases

A list of cases of resistance in mosquitoes alleged to have been caused or aggravated by agricultural insecticides is given in Table 1. The large number of *Anopheles* species involved is undoubtedly due to the fact that the susceptibility of anophelines has been followed more closely in connection with malaria eradication. It is suspected that many other cases also exist, especially in *Culex fatigans*, which remain unexamined. It is of interest to note that the majority of cases on record involve dieldrin and DDT, undoubtedly because resistance to dieldrin is known to develop readily and is easily detectable in heterozygotes and because DDT has enjoyed wider and longer use than

other classes of insecticides. However, selection by organophosphates and carbamates is also possible as evidenced by the extremely high resistance to these compounds in Anopheles albimanus in the cotton growing areas of the Pacific coast of Central America and by organophosphorus resistance in Aedes nigromaculis and C. fatigans in the heavily agricultural areas of California.

No attempt will be made to recount the specific details of every reported case since these can be found in the available literature. Reference to individual cases will be made only as supportive evidence for the criteria of implication discussed below.

Evidence of Implication

Many of the available reports are limited to merely pointing out that the problem exists in an agricultural area which is heavily treated with insecticides or that mosquito populations are more resistant in agricultural than non-agricultural areas although both have received an equal number of treatments by public health authorities. While much of this information may be convincing enough, definitive evidence comes primarily from the more comprehensive studies on An. albimanus in Central America and C. fatigans in California

The available evidence is discussed under the following categories:

1. Appearance of resistance in mosquitoes prior to use of insecticides specifically for mosquito control

2. Presence of higher resistance in mosquitoes in agricultural than non-agricultural areas.

3. Correlations between degree of resistance in mosquitoes and extent of agricultural pest control operations.

4. Correlations between seasonal levels of resistance in mosquitoes and seasonal application of insecticides to crops.

5. Correspondence between resistance spectrum in mosquitoes and types of insecticides applied to crops.

6. Evidence of suppression of mosquito population by agricultural sprays.

1. Appearance of resistance in mosquitoes prior to use of insecticides specifically for mosquito control - In Turkey, Ramsdale[5] reported that dieldrin resistance was present in An. sacharovi, An. maculipennis and An. melanoon subalpinus in many agricultural areas where neither BHC nor dieldrin have been used to spray buildings. In the delta area of Egypt, where cotton was treated extensively with toxaphene and DDT, marked resistance to dieldrin and incipient resistance to DDT were noted in An. pharoensis in 1959 prior to commencement of residual house spraying (A.R.Zahar & Thymakis, unpublished report to WHO, 1962). Between 1959 and 1962 the DDT resistance was reported to have increased greatly in non-treated areas as well as in those which received

residual house treatments, a situation which was likewise attributed to the effect of agricultural insecticides (A.R. Zahar et al., unpublished report to WHO, 1965). Similar occurrences of resistance in areas which received only agricultural sprays were reported for dieldrin in An. maculipennis in the Spineni region of Romania (M. Duport. unpublished report to WHO, 1965), An. gambiae at Bougouni, Mali[6] and in the lower Volta region of Ghana (W.Z. Coker, cited in[7]) and in An. aconitus in the Malang district of East Java in 1961[8].

2. Presence of higher resistance in mosquitoes in agricultural than non-agricultural areas - Frequently cited are reports of mosquito resistance or higher levels of it in agricultural than in not-so-agricultural areas, although both have received residual house spraying. Thus in Greece, Belios (unpublished reports to WHO, 1961) found the highest dieldrin and DDT resistance in An. sacharovi in the cotton and rice growing area of Laconia than in Etolia and Euboea, a fact which he attributed to strong selection pressure by agricultural insecticides on the larvae.

In Turkey, Ramsdale[5] pointed out in 1973 that although DDT had been widely used for more than 20 years in public health and agriculture, the incidence of DDT resistance was not related to the duration of DDT house spraying operations: more than 10 years of regular house treatment had not affected the susceptibility of An. sacharovi or An. maculipennis in the south-eastern part of the country. However, remarkable DDT resistance had developed in An. sacharovi in the cotton-growing district of Manan, Adana (M.H. Holstein, cited in [8]).

In the California pasture mosquito, Aedes nigromaculis, resistance of a lower level is frequently found in populations outside of intensively agricultural areas which are not subject to treatment by mosquito abatement authorities.

A considerable difference in susceptibility to organophosphates and carbamates occurs in field strains of An. albimanus from different areas: strains from Haiti, where agricultural use of these insecticides is minimal, are of "normal" susceptibility (generally equalling that of the long-established Gorgas reference strains) whereas strains from the cotton-growing areas of El Salvador show remarkable levels of resistance to insecticides within these groups.[9] Such differences are apparently not due to the extreme geographical separation of the populations since a strain from the isolated area of Texistipeque, Santa Ana, El Salvador, was equally susceptible to propoxur and DDT as the strain from Haiti.[10]

3. Correlations between degree of resistance in mosquitoes and extent of agricultural pest control operations - The case of involvement of agricultural insecticides in the development of resistance by mosquitoes was enhanced by the demonstration of correlations between the intensity of pest control operations on cotton and rice in areas of El Salvador and the degree of OP and carbamate resistance in An. albimanus. Cotton has been grown in the Pacific coastal plain of Central America on a large scale for over 15 years. This crop is treated with insecticides at frequent intervals, as many as 30 applications during

the 6-month growing season not being unusual. These treatments have led to development of resistance in cotton pests, thus increasing the dependence on chemicals for pest control. Mosquito resistance to chlorinated hydrocarbons and more recently to OP's and carbamates has also emerged in these areas.[11] Highest levels have been detected in the central Department of La Paz from where resistance extends at decreasing levels eastward and westward to the Honduran and Guatemalan borders. Georghiou[11] concluded that this phenomenon may be attributed to the more intensive cultivation of cotton and rice in La Paz than elsewhere in the country: "26% of the country's cotton acreage is found in the Department of La Paz. Here the average holding per cotton grower is 111.48 manzanas (1 manzana = 1.73 acres), as compared to 34.71 manzanas per grower in the remainder of the country. There are indications that the larger the holding, the greater the likelihood that insecticide treatments are applied generally on a fixed schedule rather than discriminately when and where needed. 87% of the cotton acreage in El Salvador is treated by aircraft, a practice which may be expected to result frequently in contamination of mosquito breeding habitats. In La Paz 95% of the acreage is treated by air, and approximately one-fifth of this by ultra low volume sprays."[11]

In addition to cotton, rice growing also appears to be correlated with resistance in An. albimanus. In El Salvador, according to 1969-70 statistics, 53.6% of the total rice acreage is in the central part of the coastal plain, including the Department of La Paz, as compared to 25.5% in the western and 20.9% in the eastern parts.[11] Similarly, in the Sebaco Valley of Nicaragua, where high OP and carbamate resistance has also appeared in An. albimanus, rice is the principal crop. An example of increasing dependence on insecticides for pest control on this crop is the record of treatments applied on one plantation in 1963-71 (Table 2).

As in the case of OP and carbamate resistance, DDT resistance also occurs at higher levels in the cotton growing area of Nicaragua as indicated in Fig. 1.

Additional evidence of the impact of agricultural insecticides is revealed by a study of the recent development of OP multiresistance in populations of C. fatigans in California.[12] Strains collected from dairy waste drains of two farms located 6 miles apart in the intensely agricultural San Joaquin Valley, revealed significantly different levels of OP resistance (Table 3). Both breeding sites had experienced similar larvicidal treatments applied by the local mosquito abatement district, the 1973 and 1974 treatments consisting exclusively of chlorpyrifos. However, examination of official records of agricultural insecticide applications within a 3-mile radius of each farm indicated that during 1971-74 approximately twice as large a quantity of organophosphates and carbamates had been applied to crops in the area of the more resistance population ("Camara" strain) (Table 4).

4. Correlations between seasonal levels of resistance in mosquitoes and seasonal application of insecticides to crops - A study conducted over a 2-year period in the cotton-growing area of El Salvador indicated that the susceptibility levels of An. albimanus show seasonal fluctuations in parallel with spray applications on cotton (Fig. 2).[10] Sampling was done in June and February of each year, i.e., at the beginning and end of the cotton-spraying season. Resistance to parathion, methyl parathion, malathion, fenitrothion, carbaryl and propoxur was found to rise during the spray period and to decline somewhat during the non-spray period. This escalatory pattern led to remarkably high levels of resistance by February 1972, when the study was terminated. With reference to a susceptible strain, the resistance levels observed were: malathion 117x, parathon 158x, methyl parathion 144x, fenitrothion 45x, propoxur>1000x and carbaryl 443x.[10]

5. Correspondence between resistance spectrum in mosquitoes and types of insecticides applied to crops - The El Salvador study has also indicated that the spectrum of multiresistance in An. albimanus in that country can be traced to the types of insecticides applied to cotton, by far the most common crop subject to insecticide treatments. Parathion and methyl parathion have been the principal insecticides used on this crop for over a decade. Other insecticides, including carbaryl, azinphosmethyl, trichlorphon, monocrotophos and malathion have been used to a lesser extent against specific pests. Since the geographical distribution of An. albimanus in this country coincides to a large extent with the agricultural area, data on insecticide imports into the country may be used as an approximate indication of the degree of exposure of the mosquito population to each chemical. Calculations from official records during the 10-year period 1961-70 show that 51.22% of the insecticides imported were organophosphate, 46.37% organochlorine, and 2.41% carbamate. Methyl parathion and parathion constituted the bulk of the organophosphates (93.3%) while carbaryl was the most common among the carbamates (88.1%).[10, 11] It is thus obvious that methyl parathion and parathion have had the greatest impact on An. albimanus, as reflected by the high resistance levels to these compounds. The elevated resistance to malathion may have resulted from the relatively limited malathion treatments, with additional selection of malathion-R genotypes by the other organophosphates. Carbamate resistance may be the consequence of carbaryl applications and to a lesser extent of propoxur, such resistance being supported and enhanced further by organophosphate selection pressure.

6. Evidence of suppression of mosquito population by agricultural sprays - That agricultural applications of insecticides do indeed suppress mosquito populations was also demonstrated in El Salvador.[3] Data obtained in 1972 (Fig. 3) indicated that a sharp decline of An. albimanus adult density occurs at the onset of aerial applications of insecticides to cotton in July and persists until the end of the spray period in December. In contrast, adult density was found to remain high in a non-cotton growing area some 16 kilometers distant.[3] These data thus provide direct evidence of selection pressure by agricultural sprays against mosquitoes.

Discussion and Recommendations

The available evidence leaves little doubt that agricultural insecticides, especially when applied by aircraft, are capable of exerting strong selection pressure against mosquito populations. Such pressure could be the result of decimation of the flying adult population suppression of larvae by contamination of breeding habitats or both. The consequences of such selection have been shown to be commensurate with the extent and frequency with which such exposure occurs in a given area. In the most serious case studied, El Salvador, selection occurs with regularity from August through December as shown by the large number of spray flights carried out and the nearly complete suppression of mosquito population (Fig. 3). Such selection was shown to result in the development of resistance which rises annually to higher levels in parallel with the periods of agricultural spraying. Resistance is quantitatively congruent with the intensity of agricultural operations in each area and qualitatively involves those compounds which are employed in the largest quantities in agriculture. The resultant multiresistance in the vector has considerably reduced the efficacy of residual applications of propoxur with concommitant resurgence of malaria transmission.[13]

The course of development of resistance in mosquitoes may be influenced also by the application of insecticides in public health. However, residual house spraying alone, as applied for malaria control, exerts selection pressure on only about 50% of the population since generally only female mosquitoes enter houses. Under these conditions, the possibility of resistance due to these treatments alone must be minimal. Where larvicides are used, especially in combination with residual house spraying, a higher degree of selection pressure is exerted, particularly if related chemicals are used. Exposure to both agricultural and public health treatments enhances further the prospects of resistance development. In the case of C. fatigans referred to earlier, it was concluded that the large variety of insecticides applied to crops had prepared the population to respond readily to the specific selection pressure applied by chlorpyrifos at the breeding sites. The resultant multiresistance thus contained, in addition to chlorpyrifos, the ingredients of long-standing selection by a variety of insecticides applied directly and indirectly against the population.[12]

In devising recommendations for alleviating this problem, two questions must be considered: firstly, the introduction and use of insecticides in agriculture remains unrestricted in most developing countries. New compounds are introduced before they have been fully tested and licensed in developed countries. In contrast, their use in public health, especially for residual house spraying, is preceded by exhaustive tests (e.g., WHO Testing Program[14]) over many years. Since the same compounds are usually candidates for use in both agriculture and public health, their earlier availability and use in agriculture jeopardizes their subsequent usefulness against mosquitoes.

A second consideration is the non-specific selective effect exerted on mosquitoes by the multitude of insecticides applied in agriculture. Exposure to compounds of a varied chemical nature appears to select insects with several pathways of detoxication thus preparing the population to respond more readily to subsequent specific selection.

In view of the above, the following actions are suggested as offering possible solutions:

1. Collaboration between agricultural and public health agencies and industry on the broadest possible scale for the purpose of identifying chemicals which offer the greatest promise of effectiveness against mosquitoes, and reserving these exclusively for public health use. To be effective, any agreement of this nature must be established at the highest level of authority, preferably among WHO, FAO and industry and implemented by country governments. A standing joint committee could be appointed by these organizations to review periodically the available information and to provide guidelines for action.

2. Reduction of indirect selection of mosquitoes by agricultural insecticides by the introduction of comprehensive pest management practices. It is realized that agricultural exports provide a considerable share of the foreign exchange earnings of developing countries. Thus, a reduction in the extent of insecticide usage can be expected only when alternative effective measures have been demonstrated. Since specific research is necessary to provide comprehensive pest management programs for each crop, progress in this area may be expected to be slow. Nevertheless, it is believed that the present excesses in insecticide usage can be reduced by closer collaboration between the public health and agricultural services and by an intensive program of public education.

3. Greater emphasis must be placed on the use of comprehensive mosquito control measures. The need for supplementing insecticide applications with other measures designed to reduce mosquito populations has been discussed on a number of occasions.[15-17] Such measures could contribute to reduction of mosquito density below threshold levels, at least during part of the season, thereby curtailing the number of insecticide applications needed for mosquito control. Since much mosquito breeding occurs in irrigation and runoff water, the cooperation of agriculture in effecting the necessary engineering improvements[18] (ex. drainage) and/or agronomic modifications (ex. intermittent vs. continuous irrigation of rice fields) will be required.

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Table 1. Cases of resistance to insecticides in mosquitoes precipitated by indirect selection pressure by agricultural insecticides.

Species	Country	Crop	Insecticide Resistance	Reference
Anopheles aconitus	Java	Various crops, rice	dieldrin DDT	8 25
An. albimanus	El Salvador, Nicaragua	cotton, rice	parathion me. parathion malathion fenitrothion propoxur carbaryl	9-11
	Mexico, Guatemala, El Salvador, Honduras, Nicaragua	cotton	DDT dieldrin	various (in 8)
An. gambiae s.l.	Ivory Coast	coffee, cacao	dieldrin	7
	Nigeria	ground nuts	dieldrin	22
	Ghana	cacao	dieldrin	Coker 1956 (in 7)
	Mali	cotton	dieldrin	6
	Upper Volta	cotton	DDT	Hamon *et al.*, 1968* (in 8)
	Sudan, Ethiopia, Togo, Senegal	various crops	DDT	23
An. maculipennis	Romania, Turkey	crops	dieldrin	Duport, 1965* (in 8), 5
An. melanoon subalpinus	Turkey	crops	dieldrin	5
An. melas	Zaire	bananas	DDT	24

Table 1. (continued)

Species	Country	Crop	Insectcide Resistance	Reference
An. pharoensis	Egypt	cotton	dieldrin	Zahar & Thymakis 1962* (in 8)
			DDT	Zahar, 1965* (in 8)
	Sudan	various crops	dieldrin, DDT	21
An. quadrimaculatus	USA	cotton	dieldrin	26
	Mexico	cotton	DDT, dieldrin	27
An. rufipes	Mali	cotton	dieldrin	Hamon 1968* (in 8)
An. sacharovi	Greece, Turkey	cotton, rice	DDT, dieldrin	19, 20, 5
Aedes aegypti	Tahiti	coconut	dieldrin	28
Aedes nigromaculis	USA	various crops	DDT, dieldrin, OP	Various (in 8)
Culex pipiens fatigans	USA	various crops	O-P	12

* Communications to WHO.

Table 2. Insecticide applications on rice, La Conception, Nicaragua, 1963-71[a]

Year	Insecticide Applications	Total
1963	None	0
1964	Carbaryl (4)	4
1965	Carbaryl (6)	6
1966	Carbaryl (3); Carbaryl + me-parathion (4)	7
1967	Monocrotophos (2); Carbaryl + me parathion (7)	9
1968	Monocrotophos (3); Endrin (2); Disulfoton (1); Ethyl-methyl parathion (2)	8
1969	Perthane (1); Monocrotophos (2); Endrin (2); Naled (3)	8
1970	Perthane (1); Naled (2); Bux (3); Tamaron (2)	8
1971	Naled (3); Bux (3); Tamaron (3); Diazinon (1)	10
1972	Changed to sorghum	

[a] G. P. Georghiou, unpublished

Table 3. Resistance spectra of *Culex p. fatigans* at Hanford, California, 1974 (After Georghiou *et al.* (12))

Insecticide	Susceptible Lab Strain LC_{50} (ppm)	Resistant Field Strains "Camara" Resistance Ratio	Resistant Field Strains "Knudsen" Resistance Ratio
Abate	.0018	116.7	37.2
Chlorpyrifos	.0023	52.2	27.0
Chlorpyrifos methyl	.003	83.3	40.0
Parathion	.0041	12.9	8.8
Fenthion	.0047	48.9	36.2
Methyl parathion	.005	24.0	13.4
Fenitrothion	.017	12.4	8.2
Malathion	.11	16.4	9.1
Propoxur	.35	2.7	2.7
Carbofuran	.052	2.7	
DDT	.065	6.2	5.7

Table 4. Organophosphorus and carbamate insecticides [a] applied near "Camara" and "Knudsen" dairies [b] during 1971-74 [c]. (After Georghiou *et al*. (12))

Insecticides	"Camara" Kilos (a.i.)	"Knudsen" Kilos (a.i.)
Organophosphate		
Phosmet	867	855
Parathion	936	92
Naled	506	323
Diazinon	471	67
Malathion	431	314
Monocrotophos	291	40
Methyl parathion	290	85
Dimethoate	95	32
Azinphosmethyl	70	-
Tepp	15	-
Total	3972	1808
Carbamate		
Carbaryl	629	57
Aldicarb	207	213
Carbofuran	65	75
Methomyl	43	85
Total	944	430

[a] Purely systemic insecticides not included.

[b] Each area represents approx. 93 sq. kilometers, with dairy located in center.

[c] 1974 data are for Jan.-June period only.

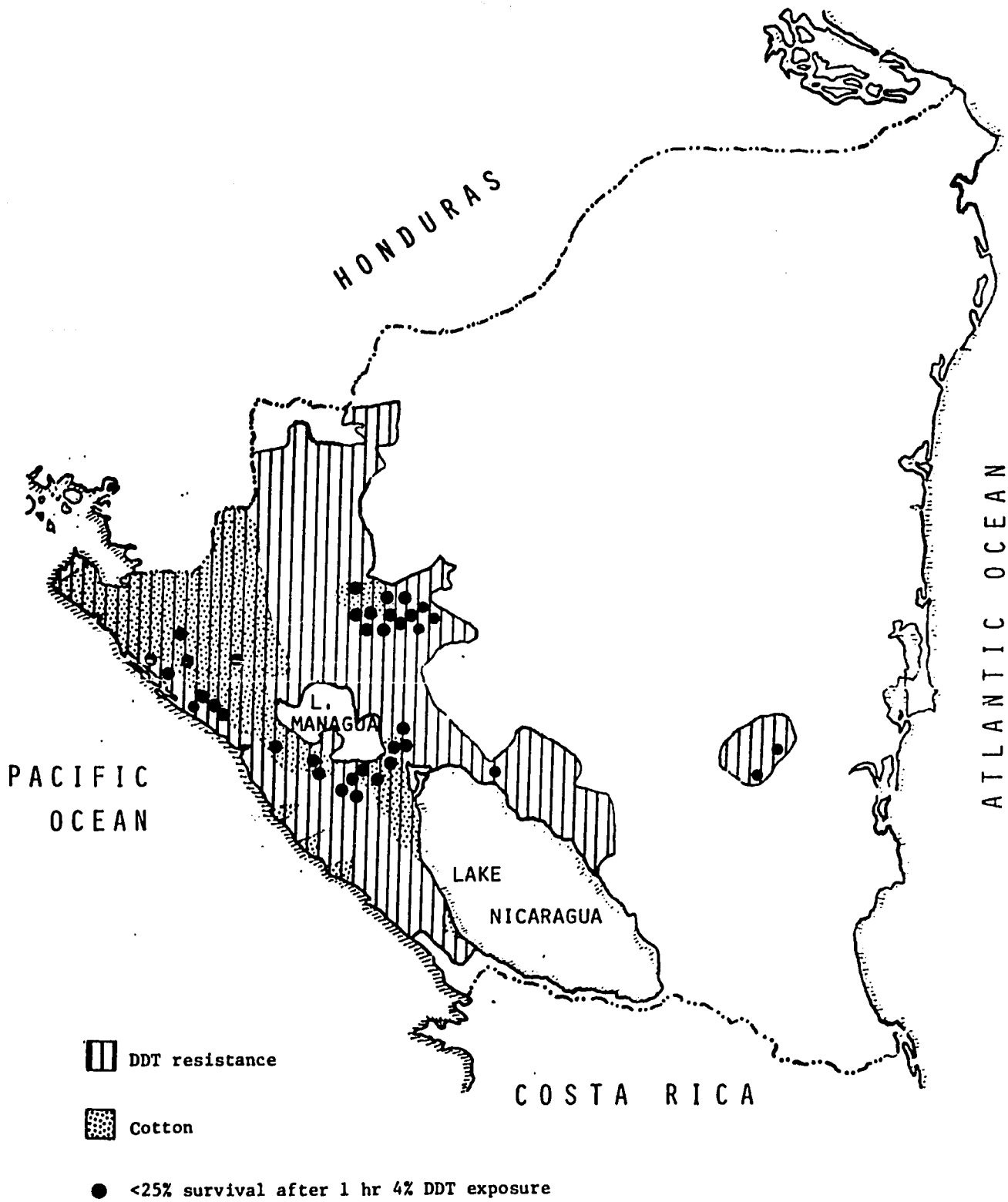

Fig. 1. Map of Nicaragua indicating geographical distribution of DDT resistance in Anopheles albimanus and cotton cultivation.

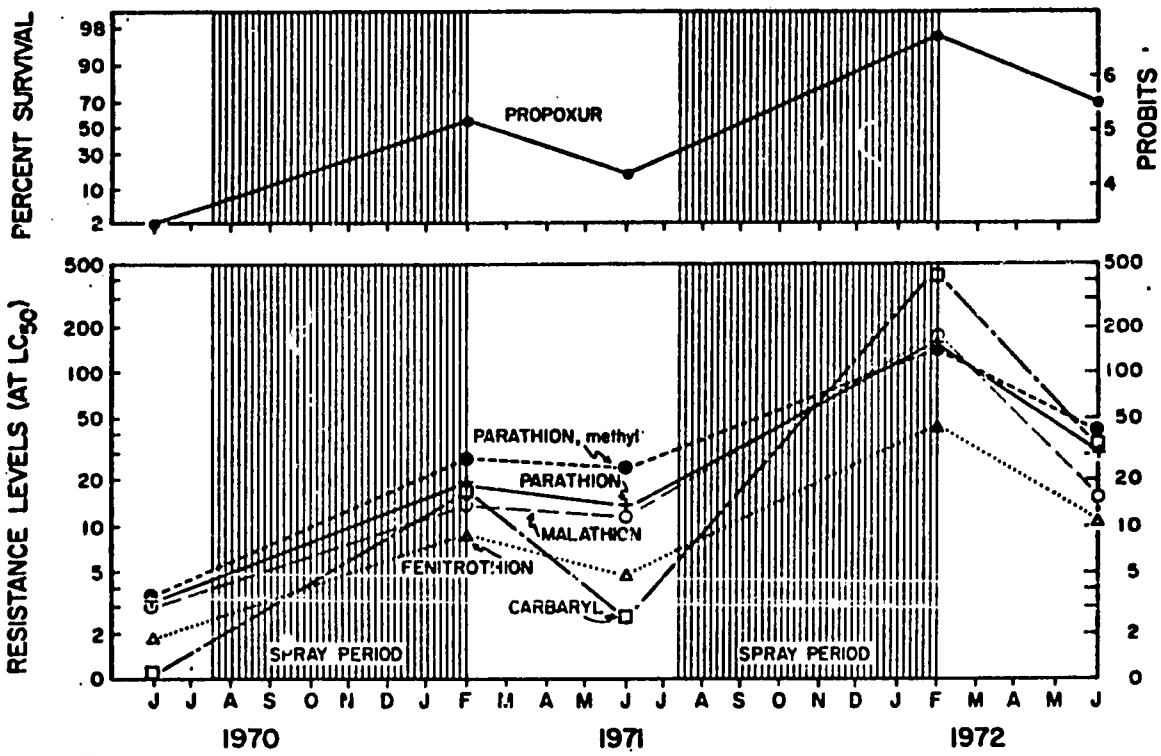

Fig. 2. Fluctuations in resistance levels toward organophosphates and carbamates in An. albimanus with reference to alternating agricultural spray and nonspray periods. [After Georghiou et al. (9)]

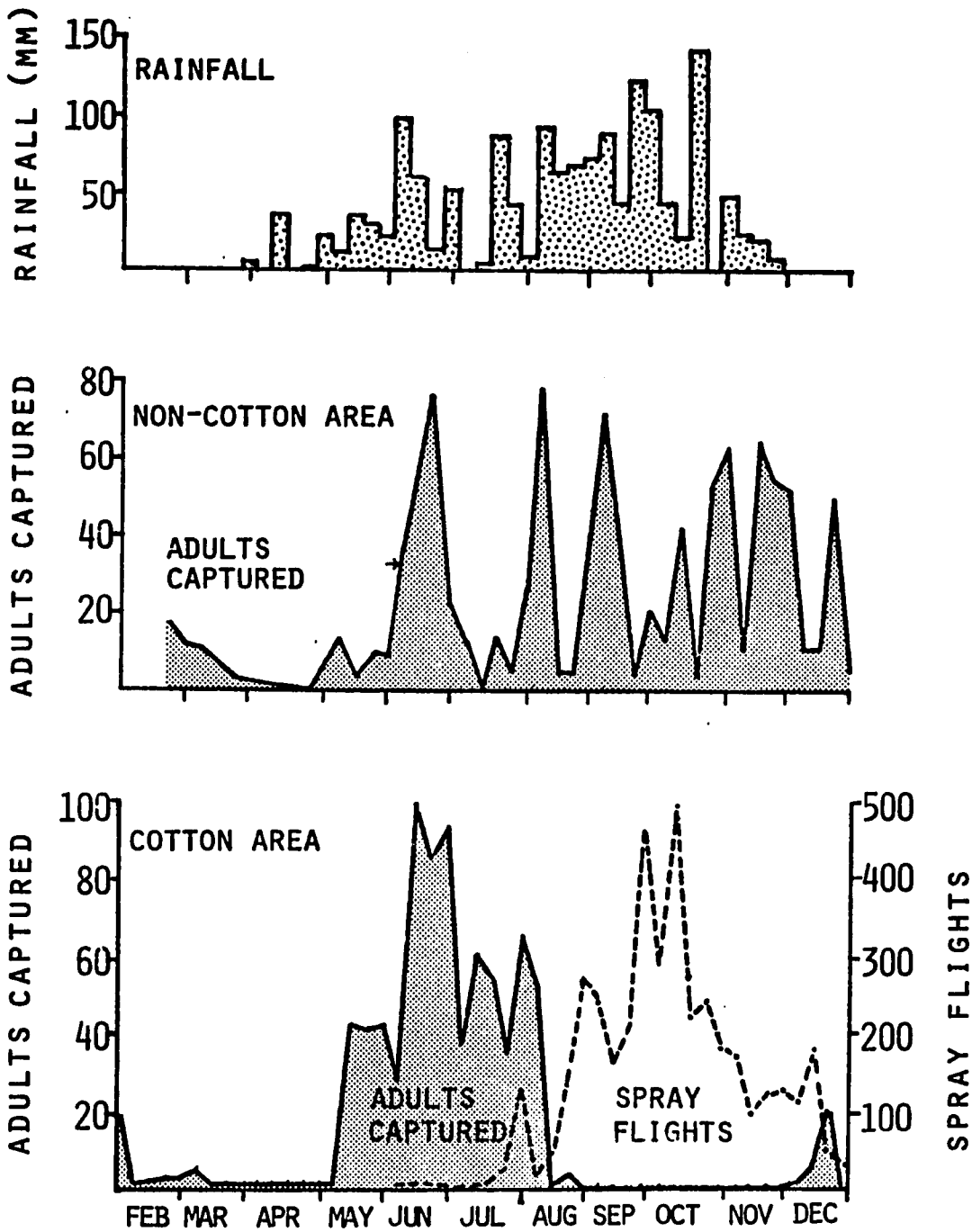

Fig. 3. Adult Anopheles albimanus densities at Melara (cotton area) and Santa Emilia (non-cotton area), El Salvador, with records of rainfall and cotton spray flights by week, in 1972. [Adapted from Hobbs (3)]

Current Medical Problems of Pesticide Management

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Presently, the medical problems of pesticide management can be categorized according to three categories of pesticide exposure representative of acute, chronic and incidental exposures. These can be figuratively presented by the iceberg shown in figure 1.

Acute Exposure

Acute exposures are reflected by incidence data of the number of pesticide poisonings occurring in various parts of the world. Incomplete statistics suggest that this is a serious problem of pesticide management, and the WHO estimates that there are approximately 500,000 cases occurring annually with a mortality rate of greater than 1% in some countries.

Poisoning victims can be divided into those who are occupationally exposed and those who are members of the general population. Occupational poisoning, which is usually the result of dermal and respiratory exposure, is milder than poisoning which is the result of accidental or suicidal ingestion. Poisonings can in turn be sub-divided into applicator poisoning and picker or residue poisoning, In the former, the worker is at some time or other exposed to the pesticide concentrate, and he becomes poisoned through this contact, during the process of manufacture, formulation, transportation, loading and application of the materials. Parathion, phosdrin, endrin and pentachlorophenol are the pesticides most commonly involved in occupational illnesses. In picker poisoning, the illness results from the contact of the worker with the foliar and soil residues of the pesticides or its more toxic oxon derivative. This phenomenon is not uncommon in the hot and arid areas of the world and is seen most frequently during the picking of citrus and cotton. Here again, parathion has been a major offender, and when this type of poisoning occurs, multiple cases rather than single cases are usually reported. Recent studies by Spear et al. suggest that physical and chemical factors which are predisposed for paraoxon formation may be the most important variable in the phenomenon of pesticide or re-entry poisoning due to parathion.

The preventive strategies which public health utilizes in these two different situations are (1) worker education and (2) routine cholinesterase testing of certain high exposure groups. Insofar as the prevention of picker poisoning is concerned, in the USA legislation for the establishment of worker "re-entry times" exists for specific pesticides. Time intervals after pesticide applications have been developed, during which intervals it is illegal for the agricultural worker to enter the field for harvesting or thinning of crops.

In contrast to occupational poisonings, accidental poisonings of the general population are the results of a wide variety of factors most of which are indicative of inadequate public education and misunderstanding of the toxicity potential of these chemicals and the dire consequences of misuse. For example, many poisonings have resulted from the ready availability of the more toxic types of pesticides in garden stores and in the "pesticide shops." They are improperly stored in the home and within reach of the toddler. Even the adult is at risk, especially if the chemical is stored in improper bottles. Overindulgence in alcohol frequently results in accidental pesticide poisoning, especially if the pesticide has been transferred to an empty gin or whisky bottle! Accidental spillage has also resulted in many cases of poisoning, and food and clothing have been contaminated during the process of transportation of food and clothing together with agricultural chemicals. The illicit use and sale of the more toxic members of this group have also resulted in human fatalities and a strict enforcement of city and provincial pesticide ordinances should be instituted. In those countries which are concerned with this problem, the introduction of appropriate pesticide legislation prohibiting the sale and use of the more toxic materials within the urban environment has greatly reduced the incidence of pesticide poisoning.

The accessibility and the utility of unwashed and undestroyed pesticide containers is another example of bad pesticide management and one which can lead to fatalities. The storage of pesticide concentrates in polyethylene bags within the metallic pesticide drum would greatly contribute to the reduction of pesticide accidents and would help prevent many inadvertent contaminations of food supplies. A massive spillage of pesticide concentrate can produce a particularly hazardous situation and several countries are now in the process of introducing emergency telephone numbers which can be contacted in such an eventuality. These centers are manned on a 24 hour basis by persons who are especially skilled in pesticide decontamination. In the USA, several pesticide companies have volunteered to provide the necessary skills and facilities for dealing with a sizeable pesticide spillage of their individual products. Animal and fish kills should also alert the appropriate authorities to the possibility of accidental environmental contamination and reports of these events should always be investigated as quickly as possible. The process of pesticide shipment and storage is another particularly hazardous phase of the distribution cycle. Careless unloading of the chemical at the dock side can result in leaking containers, and if these are stored in warehouses in close proximity to food, accidental cross-contamination may occur. Cross-contamination of food may also occur in the event of storms or floods. The general upkeep and waste disposal procedures of the pesticide storehouse is another area which should come under review and is an area which should be inspected regularly. The local pesticide industrial groups can greatly assist the local sanitary authorities in the planning and design of new storehouses.

From this short review of some of the environmental and behavioral mechanisms of pesticide poisonings, it will be apparent that this is a problem for several different agencies and institutions. Its resolution will contribute significantly to improved pesticide management, a goal which can only be achieved through effective interdisciplinary participation.

Occupational Pesticide Exposure

This is the second level of exposure, and it is an area of special concern to the physician. Occupational health and safety of the pesticide worker is receiving special attention in the US, and the EPA, NIOSH and the Department of Labor are becoming increasingly involved. Aircraft pilots, loaders, pesticide formulators and applicators have been found to be the exposed groups at greatest risk, and routine monthly cholinesterase monitoring of this sub-group is desirable. In many areas of the world, especially during harvest time, there is a tendency to employ temporary unskilled workers for pesticide loading and application. High school students and even children, in some instances, have been recruited. This must be considered to be a highly undesirable state of affairs and a practice to be condemned if there is a genuine concern for the promotion of safe and effective pesticide management. Health and agriculture should move in unison on this issue, and both should ensure that the pesticide loader and applicator is properly trained for the job and that the young, the unskilled, and the handicapped should not be entrusted with so responsible a task. This special training should not only cover the essentials for efficient pesticide application but should give equal emphasis to the steps necessary for the protection of the worker and his environment. He should receive special training in container disposal and disposal of pesticide affluent. Here again, the ingredients of good pesticide management are education, training and surveillance. These several requirements can only be implemented by the joint efforts of agriculture and health with the pesticide industry also having much to contribute by their experience in these areas. All three of these disciplines have much to gain by improvements in workers' safety. Occupational exposure is an area where there is a great need for collaborative research. For example, the use of closed systems for loading aircraft and spray tanks, the potential for new approaches to pesticide formulation and the introduction of innovative techniques in clothing need exploration. Barrier creams and clothing treatments offer considerable promise for increased worker safety.

Incidental Exposure

This is the third and last area of pesticide exposure wherein health is very deeply concerned. This type of exposure is the result of incidental exposure to pesticides through trace amounts of these materials and their metabolites in the air, in the food, in water, on clothing and in household dust.

Epidemiology of Human Pesticide Residues

This area, which represents the pesticide pollution of man, is concerned with the distribution of the persistent fat soluble pesticides. Other non-pesticide fat soluble chemicals are also appearing in widely separated communities of the world. The organochlorine pesticides most frequently identified are DDT and its metabolites, dieldrin, heptachlor epoxide and benzene hexachloride. As pesticide use changes and analytical techniques improve, new materials will appear in the human pesticide residue spectrum. Pentachlorophenol is a different type of pesticide which is being found with increasing frequency in the urine of different general population groups. The polychlor biphenyls (PCB's) are examples of non-pesticide chemicals which are detected in recent adipose population surveys. Most of the earlier monitoring studies described the prevalence of DDT and its metabolites. A sizeable body of information on the frequency distribution of this pesticide and dieldrin is on record.

The recognition that the DDT metabolites in fat were significantly correlated with residues in blood permitted the larger and more stratified sampling of communities. It was found that levels of DDT reflected recent exposure to this compound whereas levels of DDE were reflective of chronic lifetime exposures to DDT. Initially these surveys of the persistent pesticides were used to estimate national prevalences and to make internatonal comparisons of geographical differences and to estimate secular changes of these residues in man. It was first thought that DDT was homogeneously distributed throughout the general population, a distribution which was compatible with the dominant role of food as the major source of this incidental exposure. However, with the introduction of blood instead of fat as the sampling tissue, larger and more stratified sampling became possible. It soon became apparent that DDT was not homogeneously distributed in the population, and significant differences in its distribution were identified in relation to the characteristics of person, place and time. Some of these are shown in figures 2, 3, 4, 5, and 6.

In the United States, descriptive personal variables which influence the frequency distribution of total DDT levels include occupation, race, sex, age and social class. Higher levels of total DDT were found in occupationally exposed persons, in males, in people 20 years and over, in blacks when compared to whites and in the poor when compared to the affluent. Place variables show that DDT residues were higher in warmer climates, were greater in urban rather than in rural communities in some areas, and were clustered by families. Each member of a high DDT level home tended to have a higher than average level of DDT. Time variables emphasized a steady increase of DDT levels with age in persons under 20 (fig. 5), but there was a leveling off of this age effect in the over 20 (fig. 6).

These frequency distribution characteristics of DDT are not totally compatible with the concept that food is the main source for the human DDT residues and suggest that the home environment, particularly the dust in the home environment, may be an important variable of this residue in hot climates.

From a medical point of view, present concern has concentrated in three areas. These are: (1) human monitoring programs, (2) microsomal enzyme induction effects, and (3) carcinogenesis, teratogenesis and mutagenesis.

(a) Human Monitoring Studies - This issue will be discussed more fully in a later session of this symposium. However, as the list of chemicals in the human pesticide residue spectrum grows, it is obvious that medical and public health will become concerned with the need to document these subtle measures of environmental exposure. There is very little information of the yearly changes of these residues taking place in our society. Knowledge of the qualitative and quantitative characteristics of the spectrum may provide clues in the future for the study of human health effects of trace exposures to newer chemicals being introduced into our society. It is not completely satisfactory to rely on epidemiologic studies of the highly exposed worker in order to identify adverse health effects of these new chemicals. Such studies are frequently complicated by the fact that the numbers of individuals receiving high exposures which are the result of their occupation, are often too small in number to judge the health effects of the particular chemical to which they are exposed. Also, frequently many members of this work force change their jobs and are lost to follow-up. Health effects of environmental chemicals can only be identified by occupational studies if the incidence of the disease under study is very high or if the disease is extremely rare. A good example of the latter was seen recently when angiosarcoma of the liver was recognized in workers exposed to polyvinyl chloride. Liver angiosarcoma is a very rare disease so that when three cases were identified in a PVC plant in the US, it was not surprising that the hazards of this material, particularly its carcinogenic potential, was quickly recognized. For these reasons, public health is particularly interested in the establishment of a sizeable and continuing human monitoring program - a program which should be as thorough as is the food monitoring program.

(b) Liver Microsomal Enzyme Induction - The organochlorine pesticides, in common with many other drugs, alcohol and other foreign substances, are capable of inducing the liver microsomal enzymes. These enzymes are mixed function oxidase enzymes which are effective in the detoxication of a wide variety of foreign compounds. They can also alter steroid metabolism, a function which is thought to be, in part, related to the eggshell thinning property of DDT. Aldrin, dieldrin, endrin are all strong inducers and are capable of metabolizing a variety of exogeneous materials such as the aromatic hydrocarbon carcinogens. In this respect, Kay has shown that mammary tumor incidence due to dimethylbenzanthracene could be substantially reduced by DDT pre-treatment at doses of 10 and 100 ppm. Not only was tumor incidence reduced, but the induction time of DMBA tumor induction was extended. The degree of microsomal induction is within certain limits, dose related. Endrin is a strong inducer, and Jaffe et al., demonstrated significantly lower levels of serum DDE levels in workers occupationally exposed to endrin. Davies, et al., found unusually low and in some cases absent levels of DDT in patients taking diphenyl hydantoin (dilantin). They were able to remove 75-80% of adipose residues of DDT and dieldrin in nine months in volunteers to whom this drug was administered.

Although no clinical indication exists for the artificial reduction of these persistent pesticide residues in man today, this approach has certain potentials for reducing such residues in animals.

Present levels of organochlorine residues in the general population are not considered to be causally related to recognizable enzyme induction although several investigators have demonstrated enzyme induction effects in exposed workers.

(c) Carcinogenesis and Tumorigenesis - In view of the ubiquitous dissemination of pesticide chemicals, it is not surprising that scientific bodies, legislators and other interested groups have been concerned with the risk of cancer from such exposures. At present, the undisputed facts appear to be as follows:

(1) Animal studies have shown that several pesticides are tumorogenic and some marginally carcinogenic.

(2) That an incontrovertible link between pesticide chemicals and cancer in man has yet to be demonstrated.

(3) That specific epidemiologic studies have yet to be implemented which categorically prove or disprove this issue.

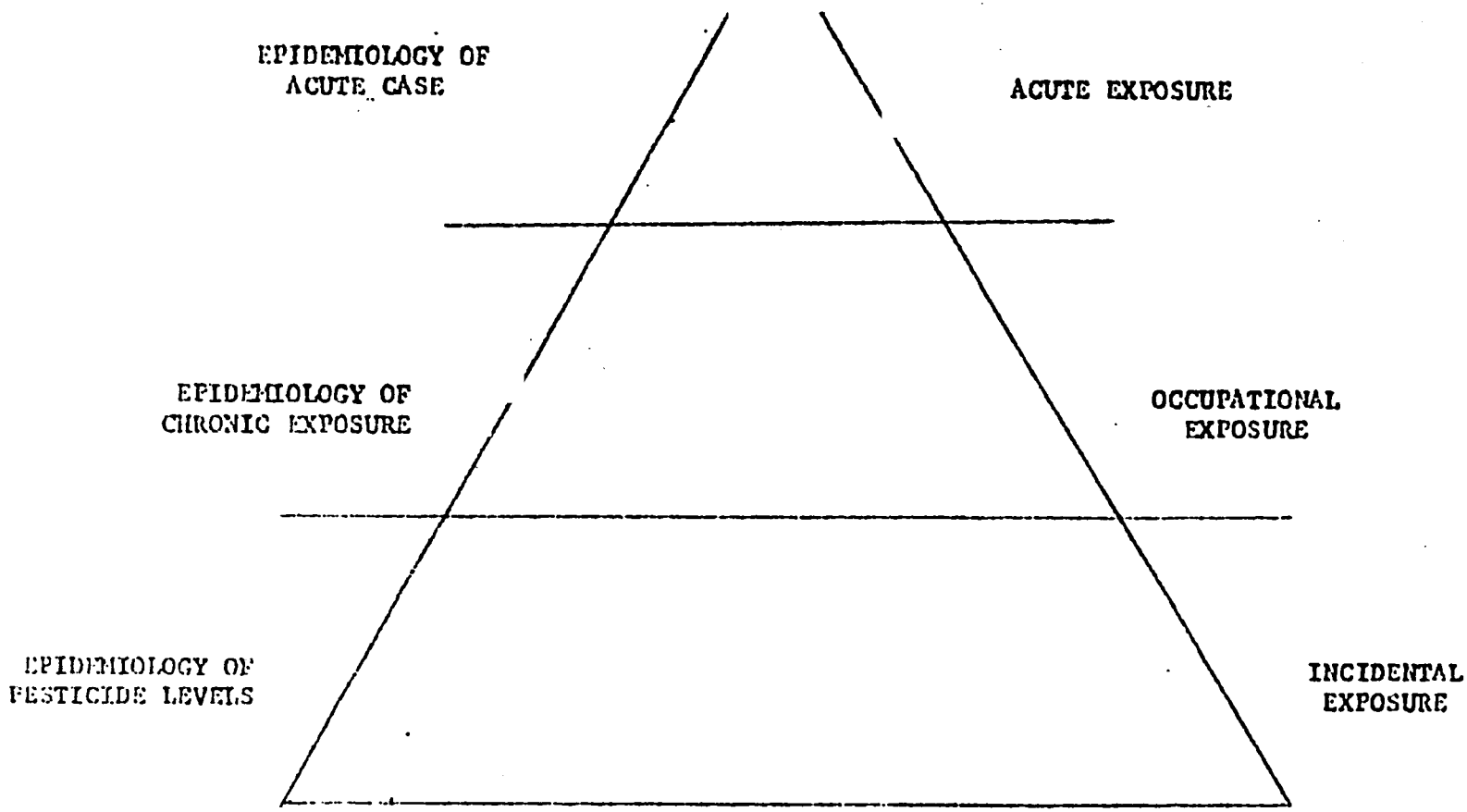
(4) That during the occupational exposure to pesticides in the processes of synthesis, formulation and application, workers are exposed to a wide variety of chemicals, some of which are tumorogenic. This work also involves exposures to powders which are used as carriers of pesticides, some of which contain asbestos and other fibrous minerals, and through use of petroleum products, to aromatic polycyclic hydrocarbons.

In a review of the occupational cancer risks of pesticide workers, Kingsley Kay considers that this group should be considered as a work group which has an occupational risk of cancer.

The last decade has seen the completion of several animal studies designed to evaluate the carcinogenic risks of a variety of pesticides. Time does not permit a review of these studies, but in summary several pesticides were shown to be tumorogenic and marginally carcinogenic in certain test animals. As an outcome of these studies, in certain countries, restrictive legislative action has followed these studies and in the USA, DDT has been banned, its use in agriculture being permitted only for selected pest problems and in limited areas of the country only. Aldrin and dieldrin have suffered a similar fate. By and large these decisions have been made on circumstantial evidence only.

Epidemiologic studies have not provided answers which have totally resolved the issue, although a review of occupationally exposed workers and case control studies of residues in cancer cases and controls have not supported the carcinogenic findings noted in animal studies.

Because the use of DDT is declining in many areas of the world because of legislative action, shortages and the growing problems of resistance, history may well show later that the issue was never totally resolved.



STRATEGY OF PESTICIDE EPIDEMIOLOGY

Figure 1

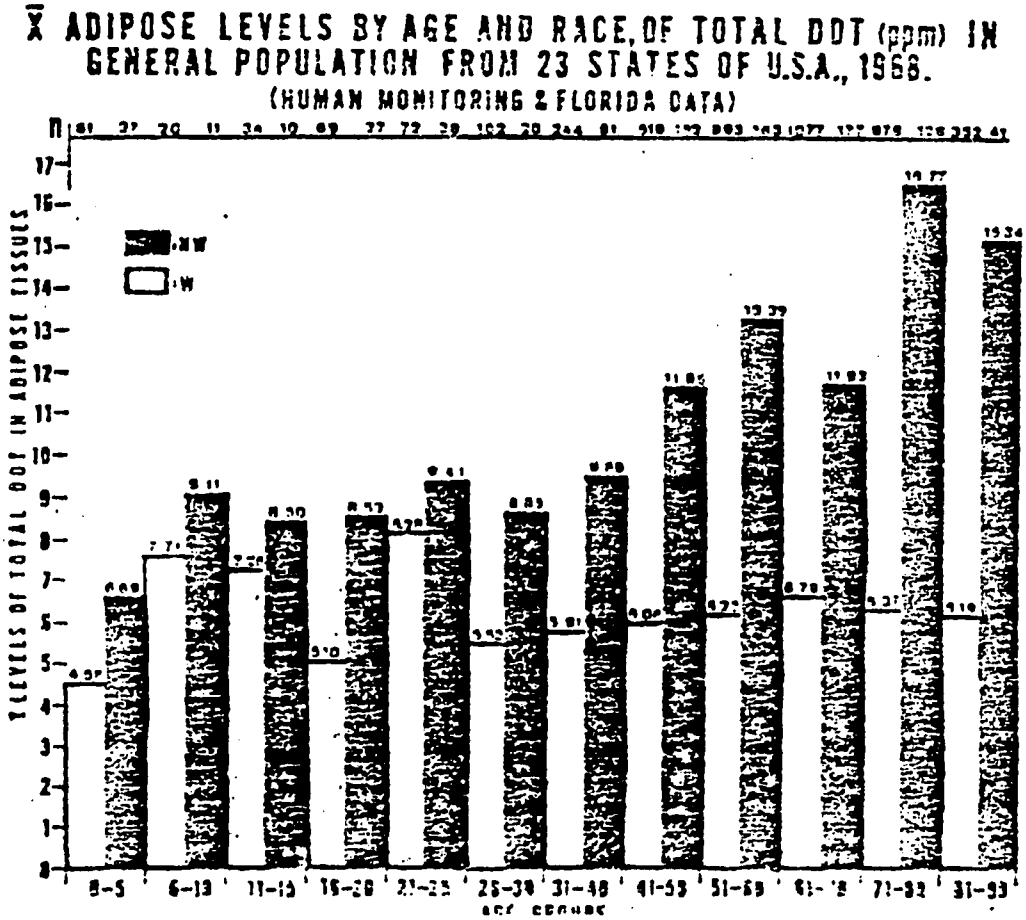
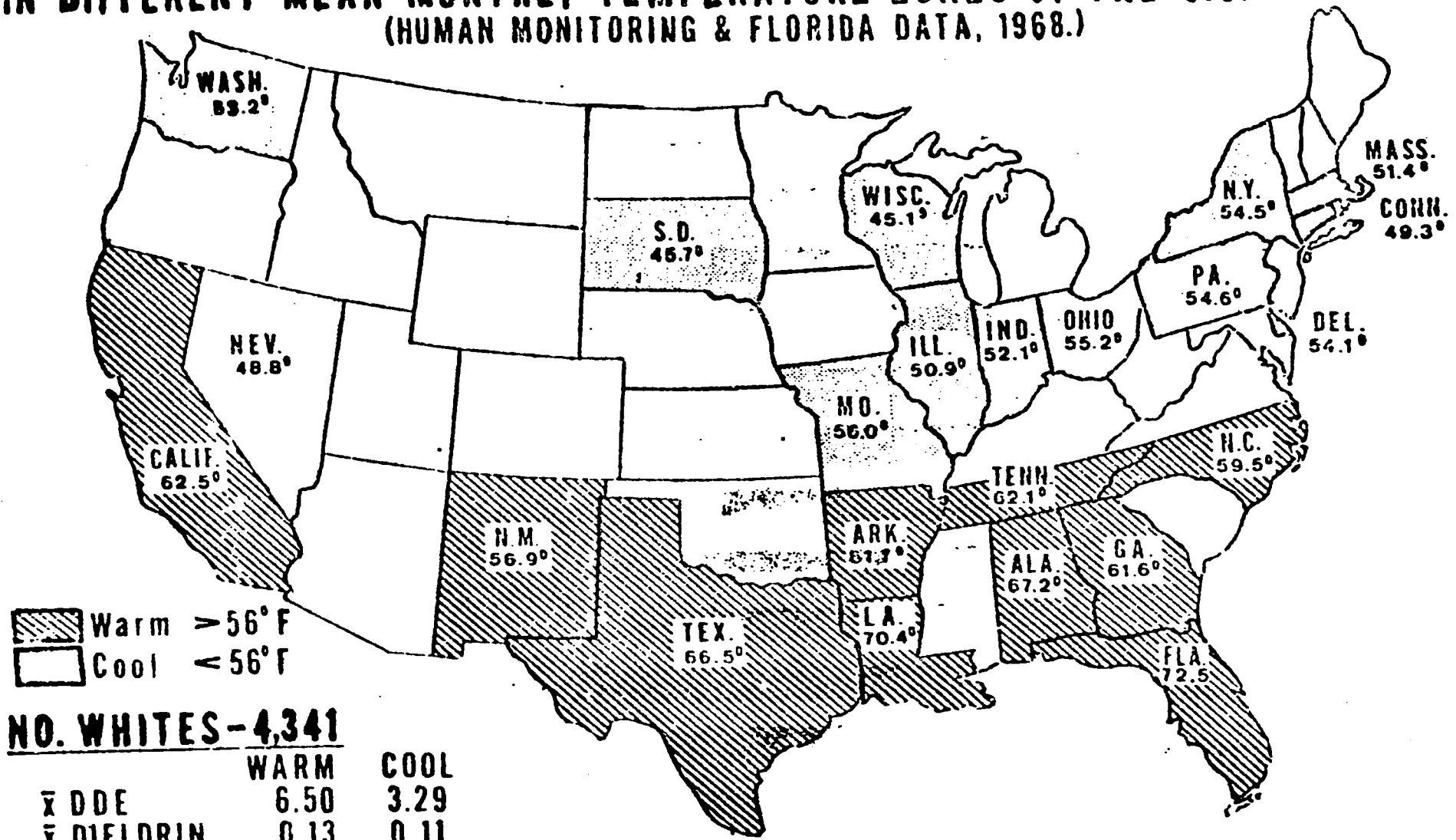

X̄ ADIPOSE LEVELS BY AGE AND RACE, OF TOTAL DDT (ppm) IN GENERAL POPULATION FROM 23 STATES OF U.S.A., 1966.
(HUMAN MONITORING & FLORIDA DATA)
n
LEVELS OF TOTAL DDT IN ADIPOSE TISSUES
NW
W
0-5
6-10
11-15
16-20
21-25
26-30
31-40
41-50
51-60
61-70
71-80
81-90

Figure 2

GEOGRAPHICAL COMPARISONS OF HUMAN ADIPOSE PESTICIDE RESIDUES (ppm) IN DIFFERENT MEAN MONTHLY TEMPERATURE ZONES OF THE U.S.A.

(HUMAN MONITORING & FLORIDA DATA, 1968.)



NO. WHITES-4,341

	WARM	COOL
$\bar{x}$ DDE	6.50	3.29
$\bar{x}$ DIELDRIN	0.13	0.11
$\bar{x}$ TOTAL DDT	9.15	4.84

NO. NEGROES-893

$\bar{x}$ DDE	9.66	5.26
$\bar{x}$ DIELDRIN	0.13	0.14
$\bar{x}$ TOTAL DDT	14.33	7.86

Figure 3

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Figure 4 - Concentrations (in ppm) of DDT-type compound and HEOD in adipose tissue in Europe; concentrations of HEOD in italics.

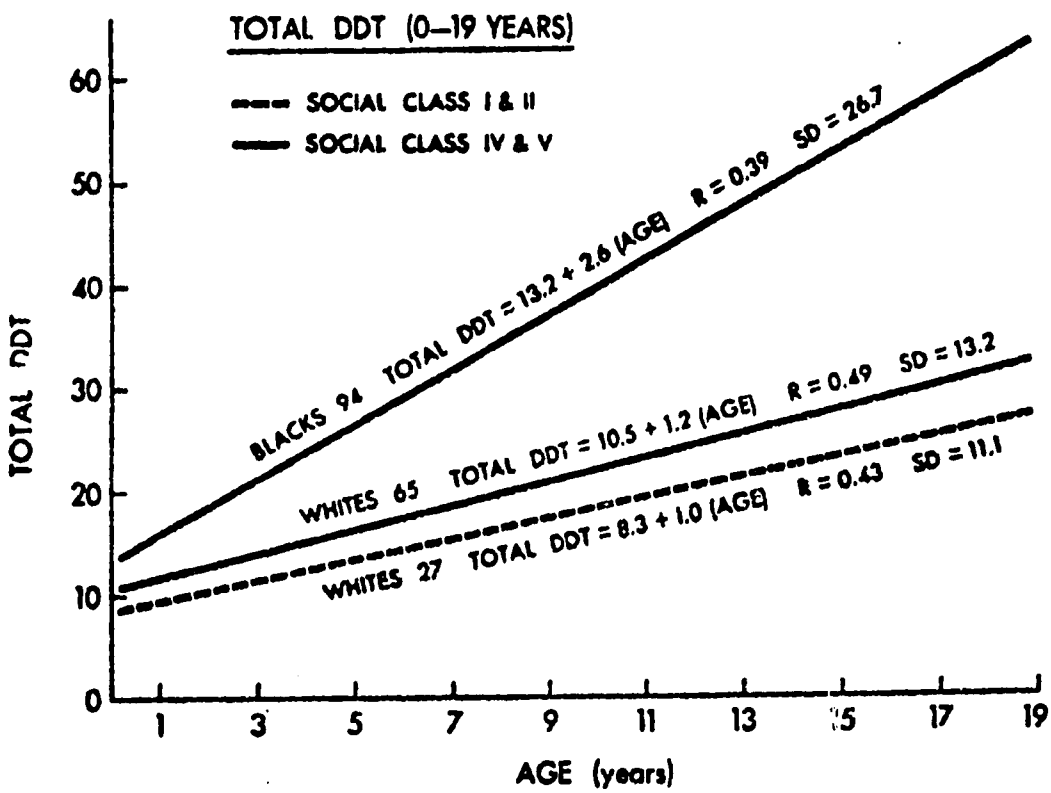

Figure 5 - Correlation of serum Total DDT levels (ppb.) in the general population of Dade County. 1971.

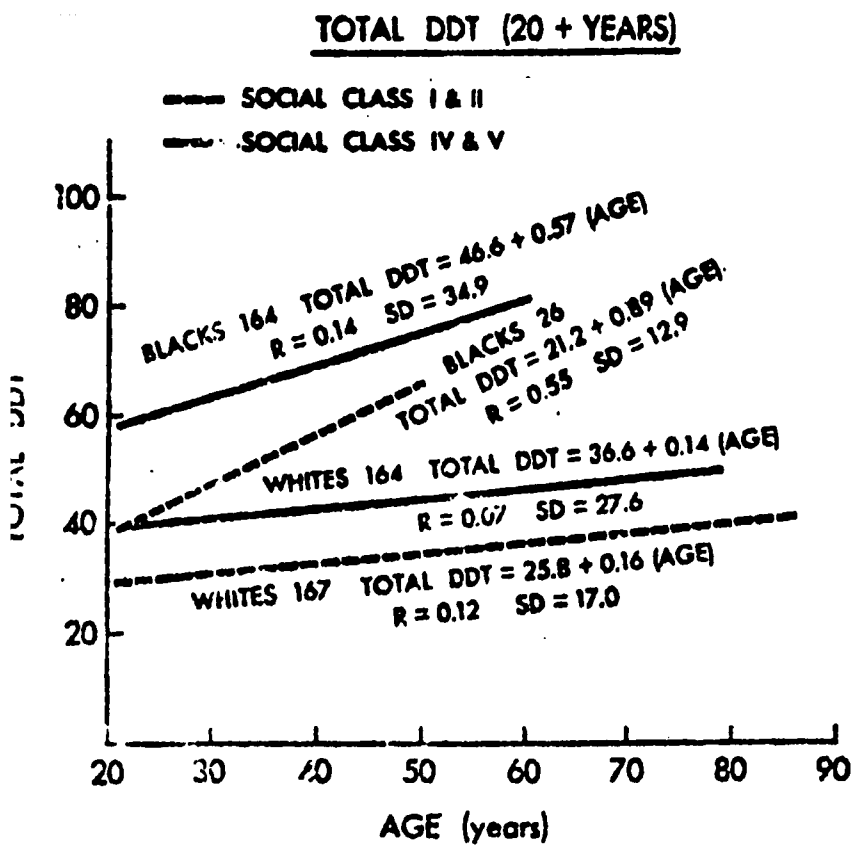

Figure 6 - Correlation of serum Total DDT levels (ppb.) with age (20-80+ years) in the general population of Dade County. 1971.

Medical Aspects of Pesticides Poisoning - Diagnosis and Treatment

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Human pesticide poisoning is a growing medical problem in many agricultural areas of the world. As a result of the problems of resistance and environmental effects of the persistent pesticides on fish and wildlife as well as for social and economic reasons, the organophosphate pesticides are replacing the organochlorine pesticides in many areas of the world. This trend, while alleviating the secondary consequences of pesticide contamination, has led to the greater use of a group of chemicals which are more acutely toxic and which require greater skills in their application if human poisoning is to be avoided.

Toxicity Vs. Hazards

From the toxicological point of view, pesticide chemicals are classified according to their oral, dermal, respiratory and delayed neurotoxicity potentials for poisoning. These various toxicity ratings, which are based upon toxicity tests on laboratory animals, list the amount of materials that are required to kill 50% of the test species (which is usually the rat) when administered by the various routes of application. Figures 1 and 2 list the LD_{50} as they are called, for some of the more commonly used organophosphate and organochlorine pesticides. The materials at the top of the list are the more toxic and the materials at the bottom of the list are the least toxic. For the organophosphates, parathion and phosdrin have been most frequently involved in human illness while endrin and dieldrin are the materials most frequently involved in human poisoning by the organochlorine group of insecticides.

This use of the LD_{50} toxicity of pesticides is of considerable use to the practicing physician because it provides him with a concept of the relative toxicity of the different materials. It is important, however, for him to recognize that this is not the only variable that is involved in human poisoning, and the concept of the hazard of the material, which is an expression of the potential of the material to produce human poisoning, must also be understood. Hazard takes into consideration such factors as the difference in oral and dermal toxicity, it reviews and

and interprets the consequences of the chemical and physical properties of the mtaerials (vapor pressure, solubility, etc.) and the methods of application and use. These differences between toxicity and hazard can be illustrated by the toxicologic records of parathion and methyl parathion. The former has an oral LD_{50} of 3-6 mg/kg and the latter 14 mg/kg, yet parathion is far more hazardous than methyl parathion. Part of the explanation for this difference is due to the fact that the Dermal LD_{50} for parathion is 6-8 mg/kg whereas the Dermal LD_{50} for methyl parathion is 67 mg/kg, and since most cases of poisoning of workers are the result of dermal exposures rather than oral exposures, it is easy to see why parathion causes more problems. This group of pesticides is broken down to oxones during their metabolism, and usually the oxone is many times more toxic than the parent compound. High temperatures favor the conversion to the oxone derivatives, and this is one of the reasons why many more pesticide poisonings occur during the warmer periods of the year. It is during these times that the rural physician should be alert for the occurrence of organophosphate poisonings. Since a detailed review of the medical aspect field of all the pesticides in current use is beyond the scope of this presentation, the clinical and therapeutic aspects of only three groups of pesticides will be discussed today. These are: (1) the anticholinesterase pesticides [organophosphates and carbamates], (2) the organochlorine insecticides, (3) Bipyridyl intoxicants [paraquat and diquat].

Organophosphate intoxication - The organophosphates are implicated in more human poisonings than any other class of pesticides. Parathion is the major offender. The clinical picture in acute poisoning can simulate pulmonary edema, myocardial infarction, diabetic coma or encephalitis. In children, intoxication has been confused with asthma, pneumonia and epilepsy. Often, an obvious pesticide exposure history is not available. Occupational exposure is largely dermal, producing a relative milder and less protracted disease than occurs after ingestion. Symptoms of illness develop within two to four hours after dermal exposure and within 15 to 60 minutes following oral ingestion.

The initial diagnosis of organophosphate poisoning must be made on clinical grounds alone. Treatment cannot be withheld pending laboratory findings. With systemic poisonings, symptoms and signs are due to cholinesterase inhibition and the appearance of muscarinic and nicotinic effects due to acetylcholine accumulation. Muscarinic effects, which usually precede nicotinic effects, include anorexia, nausea, vomiting, abdominal cramps, diarrhea, involuntary defacation and urination, sweating, salivation, lacrimation, pain in the chest with excessive bronchial secretions and blurring of vision due to miosis. Nicotinic effects include muscle twitching, fasciculations, weakness and flaccid paralysis. With involvement of the muscles of respiration, further respiratory embarrassment occurs and leads to apnea and death. Central nervous sytem signs and symptoms include anxiety, restlessness, giddiness, headache, drowsiness, convulsions and coma.

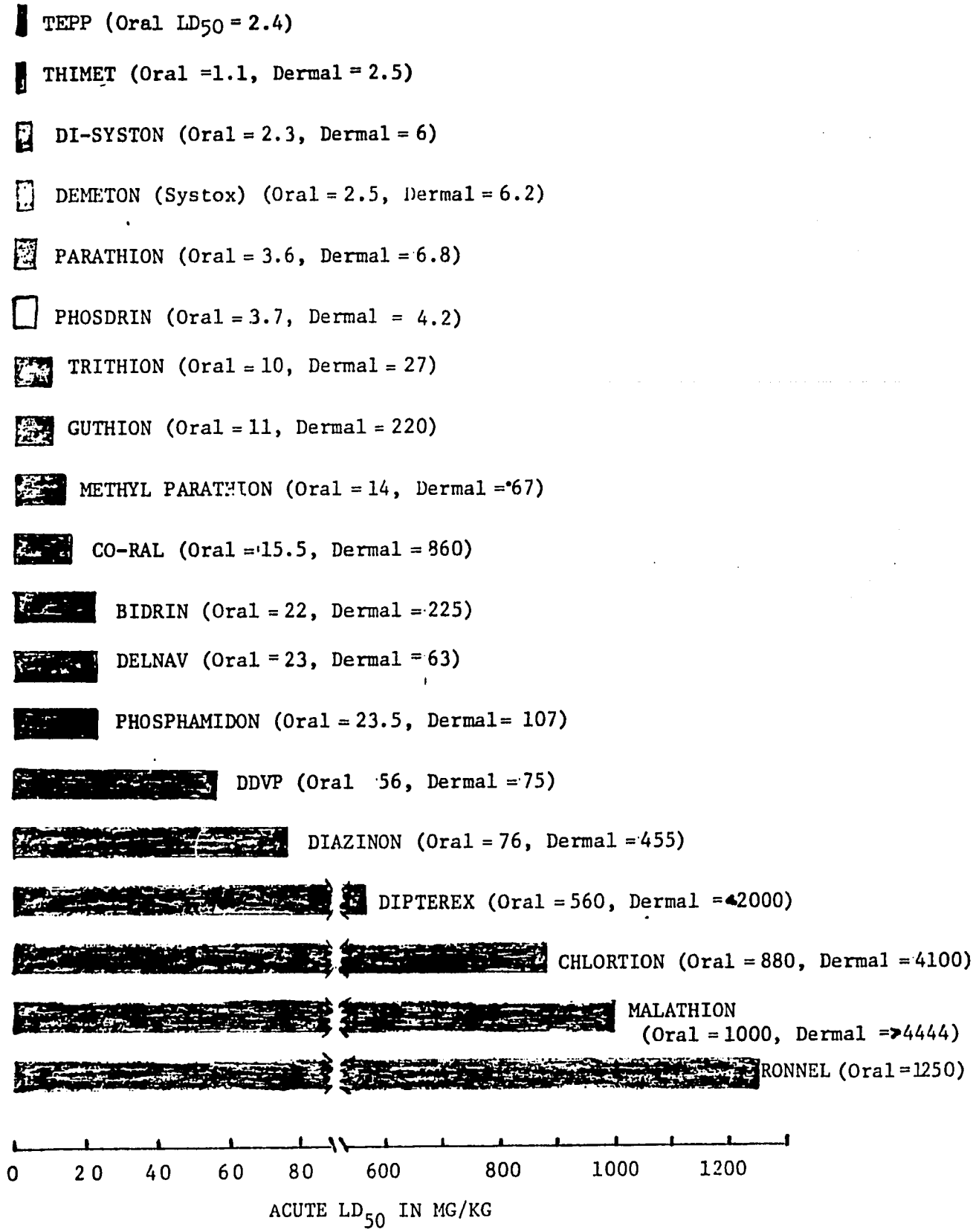

Figure 1. Graph showing acute oral and dermal toxicity values for some phosphate ester pesticides. (Prepared by the Bureau of Occupational Health, State of California Department of Public Health. Modified with permission.)

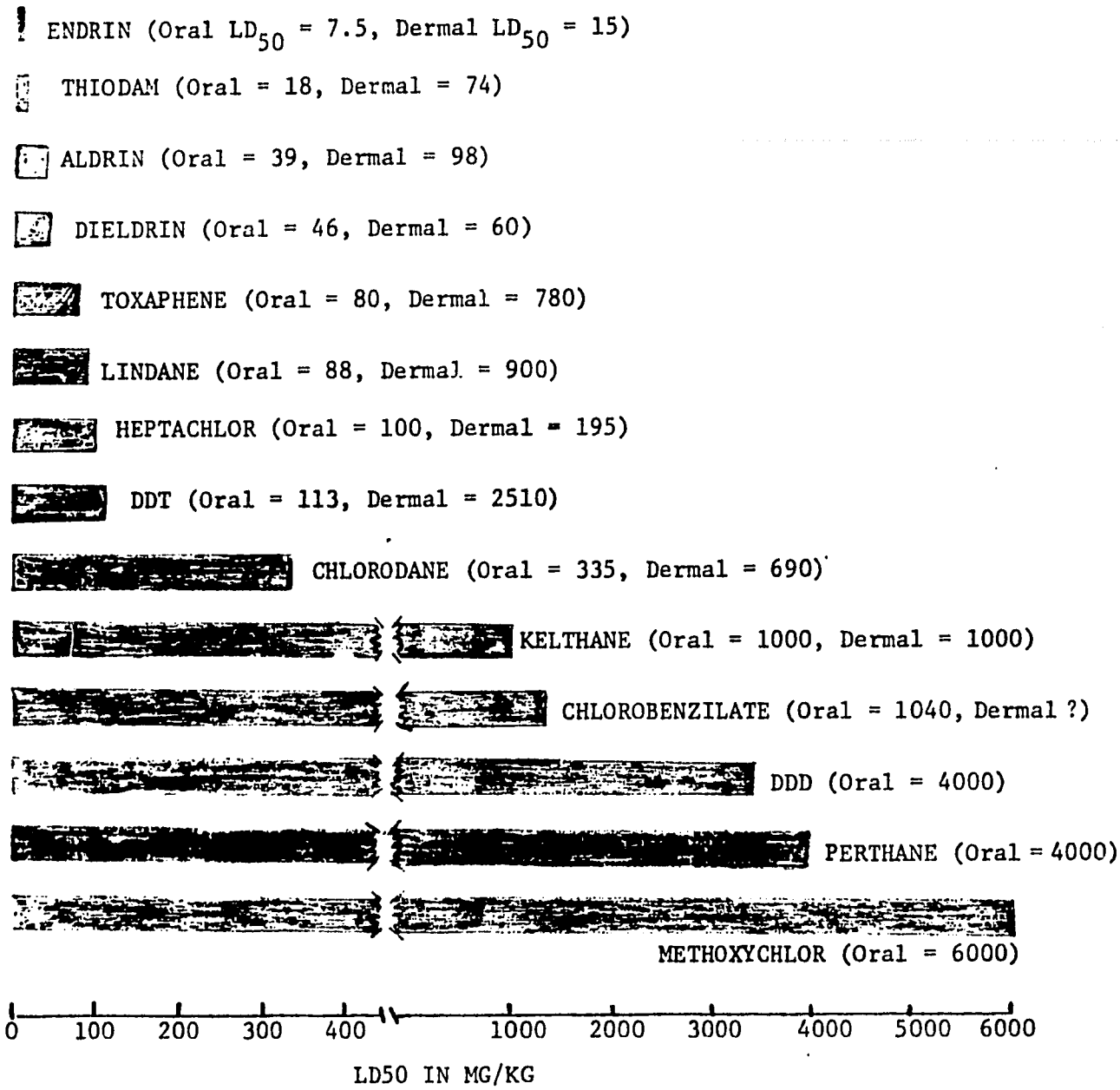

Figure 2. Graph showing acute oral and dermal toxicity values for some chlorinated hydrocarbon pesticides. (Prepared by the Bureau of Occupational Health, State of California Department of Public Health. Modified with permission.)

In the advanced state, the patient is pale, sweating and frothing at the mouth. Most frequently, the pupils are miotic and unresponsive to light, though in rare cases, dilated pupils will be seen that become miotic after starting treatment. If conscious, the patient usually is dyspneic, less commonly orthopneic, and rhonchi and coarse rales rather than crepitations are heard. Compared to the degree of respiratory embarrassment, chest x-ray findings are surprisingly minimal. Cardiovascular signs consist of techycardia and a moderate degree of hypertension; with marked hypoxia there is no hypertension. EEG abnormalities include S-T depression with flattening or inversion of T waves and atrioventricular block and idioventricular rhythm. Atrial fibrillation has also been reported. Neurological manifestations are often observed and flaccid paralyses, extensor plantar responses and electroencephalographic changes. Hypothalamic spikes were noted by Holmes; these persisted for three years after poisoning. Brown recently described two mild organophosphate poisonings that resulted in EEG disturbances of temporal lobe slowing and associated symptoms of depersonalization and the deja-vu phenomenon.

From a metabolic point of view, initial hyperglycemia and glycosuria may be observed, although the level of hyperglycemia is much less than levels associated with diabetic coma and ketoacidosis is not seen. SGOT and LDH levels may be elevated and generalized aminoacidemia and aminoaciduria have been reported. Impairment of the tubular reabsorption of phosphorus occurs but returns to normal in convalescence. There is occasionally some degree of fever with a polymorphonuclear leukocytosis. Serum electrolytes are usually normal although hypokalemia may occur and may be accentuated by diuretic therapy. This is especially problematic with the less polar but more fat soluble organophosphates such as dichlofenthion (VC 13).

Laboratory confirmation of organophosphate intoxications is provided by red blood cell (RBC) and plasma cholinesterase (ChE) determinations. Although there are numerous laboratory methods for the measurement of these enzymes, the quantitative methods used more regularly are the pH-stat (titrimetric), and the Michel (electrometric). The normal values by the Michel method for males is 0.39 - 1.20 ΔpH/hr for RBC ChE and 0.44 - 1.63 ΔpH/hr for Pl. ChE; for females the range is 0.34 - 1.10 and 0.24 - 1.54 ΔpH/hr. For the pH-stat method, the range is 8 - 17 μM/ml/min for RBC ChE and 1.2 - 5.5 μM/ml/min for Pl. ChE. In smaller hospitals, colorimetric screening tests are often used and the Acholest (Foguera) and Unipet (Pfizer) provide presumptive evidence which should be confirmed by the aforementioned quantitative methods.

The organophosphate and carbamate insecticides reduce both RBC and Pl. ChE enzymes. Rapid reactivation of ChE levels occur with carbamate intoxication, and the test for ChE inhibition may appear normal because of this. Red blood cell cholinesterase levels for confirmatory cholinesterase determinations recover shortly after oxime therapy, therefore, blood should be collected before 2-PAM is administered, in a heparinized vacutainer tube. Samples may be refrigerated, but not frozen, for a period of up to 48 hours before being analyzed. In addition to being seen after exposure to these pesticides, lowered levels

are also seen in liver disease, particularly with alcoholic cirrhosis, malnutrition, hyperpyrexia, myocardia infarction, dermatomyositis and after certain drugs. Kalow et al., have shown that 3% of the population who are otherwise normal, but who are unusually sensitive to quaternary amonium esterase inhibitors, have reduced Pl. ChE activity. These deficiencies are genetically determined and recognition of the defect is of medico-legal importance since it permits differentiation of pesticide exposure from a phenotypic mechanism. Depression of the RBC ChE can also occur in patients with paroxysmal nocturnal hemoglobinuria, disseminated sclerosis and in the newborn after complicated delivery.

Although the clinical management will vary according to the severity of the intoxication, the four essentials of treatment are: (1) restoration of the airway and correction of hypoxia, (2) atropine and oxime therapy, (2) decontamination, and (4) scene investigation and notification. Respiratory embarrassment due to secretions should be rectified at all levels. The mouth and pharynx should be cleared of secretions with a finger or by suction if available, and an oropharyngeal airway inserted; if airway obstruction persists, endotracheal intubation should be performed and the cuff inflated before gastric lavage to avoid aspiration of vomitus. Hypoxia should be corrected either with positive pressure methods or the use of 50% oxygen therapy with a nasal catheter. Serial blood gases should be drawn to monitor respiratory and metabolite dynamics.

Atropine therapy should be administered as soon as possible. Most previous reviews have recommended that cyanosis should be first corrected before commencement of atropine therapy. It is important, however, to stress that atropine is lifesaving and should not be withheld if attempts at reversing cyanosis become prolonged; in severe poisonings, atropine should be commenced while efforts are made to overcome any respiratory embarrassment. The patient is unusually tolerant to atropine and large doses may be required. The recognition of unusual atropine tolerance is an important clinical observation which helps confirm the diagnosis of organophosphate intoxication. Goetsche described a severe case of parathion poisoning in a man who was unconscious for 14 days and required atropine continuously for 18 days; the largest daily dose was 445 mg. Therapeutic failures are most often the result of undertreatment. Initially 2-4 mg is given IV and repeated every 5 to 10 minutes. The goal of treatment is to produce and maintain atropinization, with pupillary dilation and a pulse rate of 140/min. being the most important end points. Proportionately smaller doses are administered to children, but atropinization is the desired state in all cases. Occasionally, cardiac nodal refractoriness occurs, leaving the pupillary responses as the cardinal sign in atropine therapy. In such circumstances, the availability of simultaneous toxicologic information on urinary pesticide metabolites and blood pesticide levels can greatly assist the physician. Both the alkyl phosphate and phenolic metabolites have been shown to be reliable indices of organophosphate exposures. If toxicological services are available, information on the type and amount of pesticide metabolite identified in the urine will add diagnostic specificity of the exposure, provide information of the severity of the intoxication and is informative as to the need for continuing antidotal therapy by prompt identification of a pesticide poisoning.

The oximes are another group of chemicals that have a specific antidotal action in organophosphate poisoning. The only one available in the United States in N-methyl 2 formyl-pyridinium oxime, used as the chloride (2 PAM Cl) or Protopam Chloride, the bromide (2-PAM Br) and the methane sulfonate (P2S). Toxogonin is the oxime used in Europe. The major action of 2-PAM is to disrupt phosphorylated ChE, making available free ChE and promoting a loss of the dealkylated phosphoryl moiety. It relieves the neuromuscular block of muscles, particularly the muscles of respiration. Respiratory weakness, generalized muscle weakness and fatigability are markedly improved. 2-PAM should be given as early as possible and always in conjunction with atropine, the two drugs being complementary in their action. The oximes are not active against all of the organophosphate insecticides and are not recommended for use in cases of carbamate poisonings. Depending upon the particular organophosphate,"aging" of the phosphorylated enzyme occurs at which time the inhibiting enzyme can no longer be reactivated by 2-PAM. With parathion, aging does not occur for two days after exposure, so that 2-PAM may be used up to this time. With malathion, aging is early and the effects of oxime therapy in this intoxication are generally disappointing. The usual adult dose is 1 gm. IV, preferably as an infusion in 250 ml of saline given over 30 minutes. If this is not practicable, a slow IV injection of a 5% solution in water can be given over not less than two minutes. In severe cases, 2 gm. may be given initially, and a second dose of 1 gm. can be given in one hour. If convulsions are troublesome, trimethadione or thiopental may be used. Since respiratory embarrassment is usually due to excessive bronchial secretions rather than pulmonary edema, it follows that opiates, aminophylline, reserpine, phenothiazine tranquilizers, succinycholine and furosemide are contraindicated.

To decontaminate the patient, the clothes should be removed and the skin thoroughly washed with soap and water, particular attention being paid to the hair and removal of material under the nails. Because some of the pesticides are more soluble in alcohol, a second wash with alcohol is advisable. Following oral ingestion, gastric lavage is essential, the first wash being saved for toxicological studies.

It is essential that information on a pesticide poisoning be reported to the local health department of the police as soon as possible -- a telephone call is sufficient. Not infrequently, additional intoxications can be prevented by a visit to the home of the person poisoned.

Physicians having occupational health responsibilities for the pesticide worker can improve worker safety by instituting regular cholinesterase testing of those groups having significant pesticide exposure to the more toxic members of the organophosphate group. Occupational groups with the greatest work exposure include pesticide applicators, loaders and mixers, pilots and pesticide formulators. In our laboratory, a red blood cell cholinesterase level of 0.40ΔpH/hr has provided a workable cutoff point for temporary withdrawal of the worker from further organophosphate exposure.

Organochlorine Intoxication

In contrast to most of the organophosphates, the organochlorine class of pesticides exhibits features both of toxicity and persistence. There is a wide range of toxicity in the various members of this group; most reports of chemical toxicity have followed endrin, dieldrin, lindane and chlordane exposure. Illness is usually the result of accidental or suicidal ingestion of the concentrate, although occupational intoxication has also resulted from dieldrin exposure in the field and during manufacture.

Poisoning symptoms are largely due to central nervous system stimulation, but include also effects in liver, lung, kidney and blood vessels. Absorption is oral and dermal. Paresthesias, dizziness, ataxia, tremors and convulsions occur. Electroencephalographic changes reflective of brain-stem stimuli are noted and usually precede seizures. These changes involve bilateral synchronous theta waves and occasional bilateral synchronous spike and wave complexes. They return to normal after withdrawal from exposure. Basically, two patterns of seizures have been described. One is the sudden onset of seizures with no prodrome -- these are typical of endrin poisoning. Coble et al. described such a case in a woman who first presented with a hemotoma, having no knowledge that she had previously sustained a convulsion which caused it and which was due to endrin poisoning. Muscle twitching, myoclonic jerks and convulsions preceded by heacache, drowsiness, nausea and vomiting constitute the other pattern, most commonly seen with aldrin and dieldrin poisonings. In severe cases, death is usually due to respiratory depression but may also be due to asphyxia during convulsions, ventricular fibrillation and renal failure. Chronic exposure may produce peripheral neuritis. Organochlorine studies taken at or shortly after intoxication help confirm the diagnosis. Since in the rat the severity of intoxication was correlated with brain concentrations and since blood is more closely in equilibrium with the brain than adipose tissue, blood levels are more diagnostic of poisoning than fat levels.

In Asia, although information is incomplete, the organochlorines appear to cause more illness than organophosphates. Ceylon, from 1960-63 had 313 organophosphate and 481 organochlorine poisonings. Several epidemics of endrin poisoning have been documented. In Arabia, in 1967, there were 874 poisonings with 26 fatalities. In a survey for the WHO in Indonesia, the author obtained information on 31 organophosphate and 478 organochlorine poisonings. Reports of individual cases and epidemics were encountered. As in Arabia, most were the result of accidental contamination of common foodstuffs such as flour and rice, often through the illicit use of discarded drums or because of leakage of these in transit, with seepage into adjoining food. Another hazard recognized was the potential for cross-contamination of food and pesticides in adjoining buildings by flood waters during the monsoon period. Epidemics of poisonings could be seen by reports of clusters of convulsive seizures, with or without preceding gastro-intestinal symptoms; cases were confirmed by retrospective epidemiologic investigations and toxicologic studies.

The clinical management of organochlorine poisonings is symptomatic. Following gastric lavage, CNS sedation should be initiated as rapidly as possible with such drugs as barbiturates and diphenylhydantoin. Morphine and epinephrine are contra-indicated. An intravenous drip of succinylcholine chloride, intubation and respiration with 40% oxygen has proved effective in management of continued seizures.

Bipyridyl Intoxication

Paraquat (1-1 dimethyl 4,4-dipyridylium dimethyl-sulfate) and diquat (1,1'-ethylene-2,2'-bipyridylium) are two bipyridyls that are widely used in agriculture for weed control and defoliation. Paraquat is more toxic than diquat and produces proliferative changes in the lung, cornea, lens, nasal mucosa, skin and fingernails.

Diquat affects the lens and gastrointestinal mucosa and does not provude the lung changes characteristic of paraquat. Except for eye lesions, illness due to occupational exposure is usually mild and is the result of topical exposure. Epistaxis occurs in workers following droplet inhalation, and conjunctival changes occur with accidental spillage.

Very different is the clinical picture following accidental or suicidal ingestion. Although there are a few reports of recovery following ingestion, most paraquat intoxications are fatal, and their management is unsatisfactory and largely symptomatic. Following ingestion of an amount as small as an ounce of paraquat, three clinical stages are recognized. First, there is a gastrointestinal phase with burning in the mouth and throat, nausea, vomiting and abdominal pain with diarrhea. Next, usually several days after exposure, signs of hepatic and renal toxicity appear. These are due to a central zone necrosis in the liver and acute tubular necrosis of the kidney. Ten to twenty days after ingestions, progressive proliferative changes in the lungs develop. Hyperplastic changes in the terminal bronchioles occur with alveolar fibroblastic proliferation. Loss of lung surfactant has been demonstrated. Within a few days, death from respiratory failure occurs. These severe and relentless pulmonary changes were also noted in a patient who had injected himself with paraquat as a suicidal gesture.

Urine studies in animals and patients indicated that 90% of the ingested paraquat is excreted in the first 24 hours. Delayed pulmonary effects appear to be the result of an irreversible process that develops long after the initial stimulus has gone.

Paraquat is poorly absorbed from the gut. Excretion data suggest than only 1-5% of the ingested material is absorbed in man, but maximal blood concentrations are reached within 4 to 6 hours after ingestion. Treatment in man is directed toward: (1) attempts at limiting the amount of material absorbed, and (2) steps to promote the elimination of paraquat from the body. The adsorptive properties of Bentonite, Fuller's earth and other clays on bypyridal absorption have been studied in cats and rats; the

first two prevented poisoning in rats and reduced absorption in cats. Fuller's earth (30%) was more effective than Bentonite. Early administration of these adsorbents is essential and should be combined with gastric lavage. Diuresis should be forced with manitol. Peritoneal dialysis is required for renal failure. Although steroids and antibiotics are given for pulmonary complications, no treatment has been shown to be effective in the management of this phase of the intoxication.

Chemistry of Pesticides

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Pesticides are often classified biologically, i.e., on the basis of the organism which the compound controls. Thus, we have insecticides, miticides, herbicides, fungicides, etc. It is also useful to classify the many compounds used as pesticides on a chemical basis. Related compounds, whether they be insecticides or fungicides, would thus have similar chemical characteristics which would determine how the compound might behave in the environment, how it might be metabolized by some organism or what procedures might be adapted for its analysis. The large majority of compounds used as pesticides are organic, and thus classification would be based primarily on the nature of the functional groups which characterize the compound.

Chlorinated Hydrocarbons - A large variety of pesticidal compounds are usually included in this group whose major characteristic is that the compound has numerous chlorine substituents and few, if any, other functional groups in the molecule. For example, the fungicide hexachlorobenzene would be included in this class. The most renowned pesticide in the group would be DDT. Its effectiveness prompted the development of a series of chlorinated compounds with this basic structure (diphenyl ethane), such as methoxychlor and dicofol.

Aldrin, dieldrin and endrin have a different carbon skeleton than DDT but would also be classified as chlorinated hydrocarbons. Heptachlor and chlordane have somewhat similar structures. Toxaphene would also be included in this group; however, the commercial preparation is a mixture of compounds derived from the chlorination of camphene. The different components of the mixture would vary in the number and location of chlorine substituents. Benzene hexachloride -- an unfortunate name since the compound is more correctly hexachloracyclohexane, is an alicyclic rather than an aromatic compound. However, one could also classify this pesticide as a chlorinated hydrocarbon.

Thus, a rather diverse group of molecular structures is included in this class of pesticides. The chlorine substituent is relatively unreactive and the C-Cl bond relatively non-polar. Thus, we find that these compounds often are fairly resistant to breakdown with comparatively low water solubility (sometimes in the ppb range) and high partition coefficients, and consequently tend to partition into hydrophobic environments such as organic matter of soil or fat deposits in animals.

Organophosphates - These compounds -- mostly insecticides -- are esters of phosphoric acid. TEPP, for example, is a simple ester of pyrophosphoric acid and ethanol, while dichlorvos is an ester of orthophosphoric acid. The more widely used organophosphates (e.g., parathion, diazinon, etc.) are variants on the basic phosphate structure in that one of the phosphate oxygens is replaced by sulfur. Malathion, on the other hand, is a dithiophosphate in which two phosphate oxygen atoms have been replaced with sulfur atoms.

Phosphate esters -- like any other ester -- will hydrolyze (react with H_2O) to give ultimately the phosphoric acid and corresponding alcohols (or thiols). Thus, in contrast to chlorinated hydrocarbons, organophosphates break down fairly rapidly. The phosphate or thiophosphate portion of the molecule confers some polarity on the molecule, and so we find that these compounds tend to be somewhat more water soluble and give lower partition coefficients than the chlorinated hydrocarbons. It should be emphasized that both rates of breakdown and partition coefficients vary markedly with the nature of the different substituents on the phosphate moiety so that a compound such as leptophos with several aromatic substituents in the molecule shows as high a partition coefficient as DDT.

Carbamates - These pesticides are derivatives of carbamic acid. Esterification of the acidic function and substitution on the nitrogen gives compounds such as the herbicide IPC and the well known insecticides, carbaryl and propoxur. Substitution of sulfur for oxygen produces a thiocarbamate such as the herbicide EPTC.

Like the organophosphates, these compounds hydrolyze readily at the carbamate linkage and thus degrade fairly rapidly. Those carbamates containing aromatic rings have fairly low solubilities (10-100 ppm) while the alkyl carbamates will have solubilities in the range of 100-1000 ppm.

Phenols - Pentachlorophenol and DNOC are examples of this series of compounds which find use as fungicides, herbicides and insecticides. These compounds are weak acids, and consequently their behavior will vary with the pH. The salt or anion, predominant at pH values greater than the pK, is more water soluble and less volatile than the undissociated phenol.

Phenoxyacids and Benzoic Acids - A number of herbicides have been developed which are relatives of 2,4-D, a phenoxyacetic acid. Substituted benzoic acids also are finding use as herbicides. The chemical properties of these compounds vary drastically depending on whether the compounds are used as a salt, the free acid or an ester. The salts will be water soluble and not volatile, while the free acid and esters tend to be less soluble and more volatile. With the esters, volatility decreases with the molecular weight of the alcohol, i.e., butyl ester is less volatile than the propyl ester.

Ureas - The substituted ureas such as monuron and diuron are organic bases which bear some structural resemblance to carbamates. The ureas are water soluble to the extent of 5-3000 ppm -- depending on the size of the non-polar substituents on the nitrogen and also breakdown by hydrolysis.

Chemistry of Pesticides

Ian J. Tinsley
Department of Agricultural Chemistry
Oregon State University
Corvallis, Oregon

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Nitrogen Heterocyclics. Heterocyclic compounds contain atoms other than carbon in the ring structure and a series of herbicides have been developed which vary both in the ring size and the number of nitrogen atoms in the ring. Amitrole, for example, is based on a 5-membered ring containing 3 nitrogens, while the common triazine compounds, such as atrazine and simazine, are based on a 6-membered ring containing 3 nitrogens. Picloram on the other hand contains a 6-membered ring with only one nitrogen.

These cyclic compounds are quite stable, particularly the triazines, and consequently are very persistent. Triazine water solubility ranges from 5-700 ppm. Because these are bases their behavior will also vary with pH. Paraquat could also be included in this class of compounds; however, the quaternary or charged nitrogen confers rather unique properties on this compound. It is a salt.

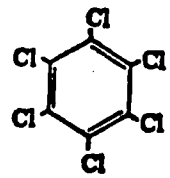
Simple Aliphatics. Many of the common fungicides are simple molecules, such as methyl bromide, EDB (ethylene dibromide) or DD (dichloropropene). These compounds of low molecular weight will have high vapor pressures which are essential to their fumigant action. The herbicide dalapon could also be included in this class because it is a rather simple aliphatic acid.

Organometallic Compounds. A number of compounds which contain covalently bound metals find use as pesticides. Organic mercury compounds have found extensive use as fungicides and compounds such as cacodylic acid have been widely used as herbicides. More recently organo-tin compounds, such as cyhexatin, have been introduced as miticides. Chemical characteristics of these compounds are more indicative of organic rather than inorganic compounds; for example, they tend to be quite fat soluble and are metabolized much like organic compounds.

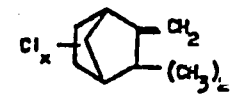
Any classification system is imperfect and the various classes above would exclude such compounds as propanil, a derivative of aniline, or endothal, the sodium salt of a simple cyclic di-carboxylic acid. Nor would the classification include the rather complex structures of the naturally occurring insecticides rotenone or pyrethrin. The naturally occurring compound, nicotine, would classify as a nitrogen heterocyclic. However, the major classes of compounds are included--that is a certain structural or functional feature which provides the basis for a series of active, commercially used compounds--and the major quantities of pesticides used would also be covered by these classes.

CHLORINATED HYDROCARBONS

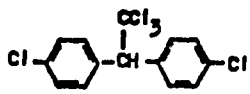
HEXACHLOROBENZENE



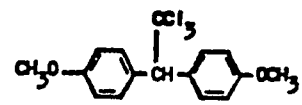
TOXAPHENE



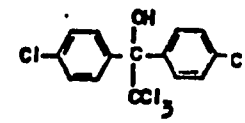
DDT



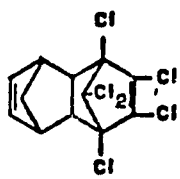
METHOXYCHLOR



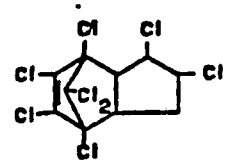
DICOFOL



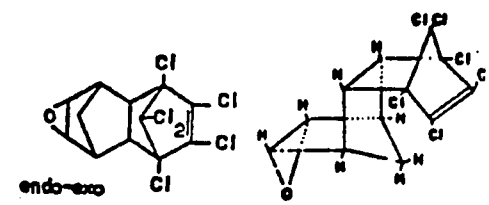
ALDRIN



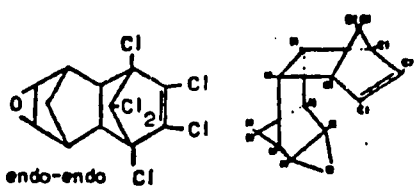
CHLORDANE



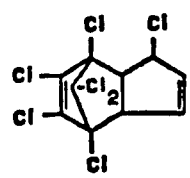
DIELDRIN



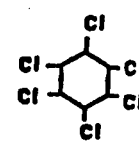
ENDRIN



HEPTACHLOR

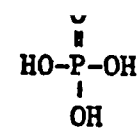


HCH (BHC)

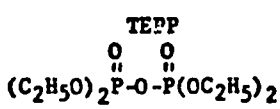


ORGANOPHOSPHATES

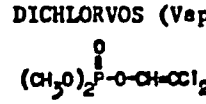
PHOSPHORIC ACID



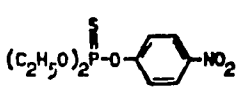
TEPP



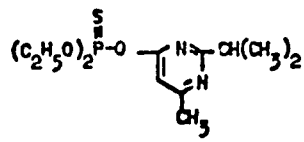
DICHLORVOS (Vapona®)



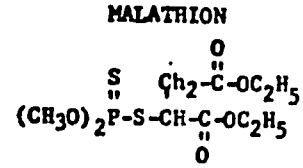
ETHYL PARATHION



DIAZINON

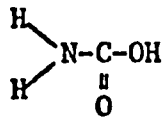


MALATHION

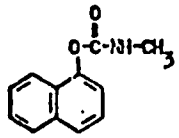


CARBAMATES

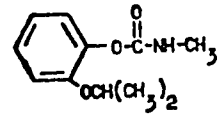
CARBAMIC ACID



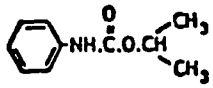
CARBARYL (Sevin®)



PROPOXUR (Baygon®)



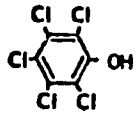
PROPHAM



EPTC

PHENOLS

PCP



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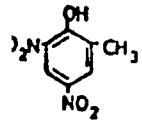
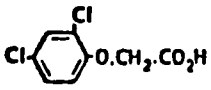
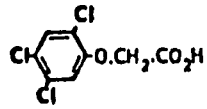


PHENOXY ACIDS - BENZOIC ACIDS

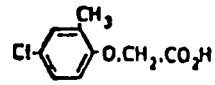
2,4-D



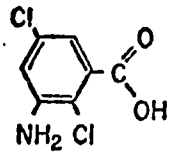
2,4,5-T



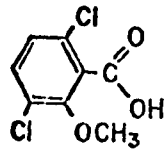
MCPA



AMIBEN



DICAMBA



UREAS

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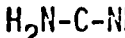
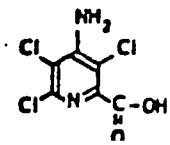


MONURON

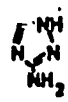
DIURON

NITROGEN HETEROCYCLIC COMPOUNDS

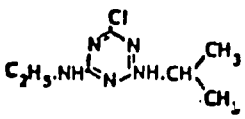
PICLORAM



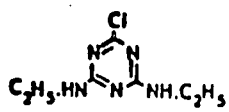
AMITROLE



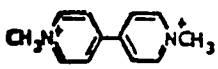
ATRAZINE



SIMAZINE



PARAQUAT



SIMPLE ALIPHATICS

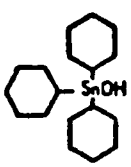
METHYL BROMIDE	EDB	DD	DALAPON
CH_3Br	CH_2BrCH_2Br	$CH_2Cl-CH=CHCl$	$CH_3-C(Cl)_2-COOH$

ORGANOMETALLIC COMPOUNDS

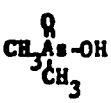
PANOGEN

$CH_3-Hg-NH-C(=NH)-NH-C\equiv N$

Plictran®

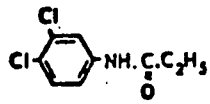


CACODYLIC ACID

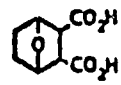


MISCELLANEOUS

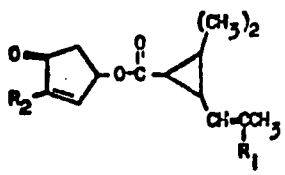
PROPANIL



ENDOTHALL



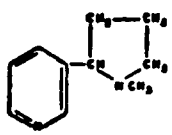
PYRETHRIN



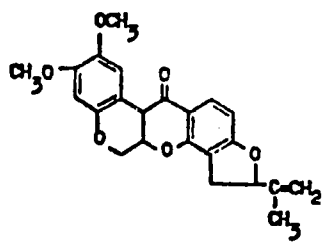
Pyrethrin I:
$R_1 = -CH_3$
$R_2 = -CH_2CH{=}CHCH{=}CH_2$

Pyrethrin II:
$R_1 = -C(=O)-OCH_3$
$R_2 = -CH_2CH{=}CHCH{=}CH_2$

NICOTINE



ROTENONE



ANALYSIS OF PESTICIDE RESIDUES

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The use of pesticides in agriculture will result in residues on the crop. The level of this residue in the consumable portion must be kept below concentrations which could prove to be harmful to the consumer. This is accomplished by controlling both the rate and time of pesticide application. The information necessary to make such decisions depends upon a knowledge of the amount of pesticide required to control the pest, as well as analytical information which will indicate how much residue is produced by certain rates of application over different time intervals. Obviously, this type of information must be accumulated before recommendations are prepared for the use of a given compound in a specific crop.

Once the particular pesticide is being used commercially it is necessary for the government regulatory agencies to do some monitoring to insure that the regulations are being followed and to confirm that the recommendations made were effective. The need for reliable analytical methods for pesticide residues in this phase of pesticide technology is thus quite obvious.

The ability to analyze for pesticide residues is important in other situations, such as the question of deciding what succession of crops may be planted in a certain field. For example, corn may be grown in a field and a herbicide program followed to control the undesirable plant species. Residues of these herbicides may persist and the question arises as to whether some crop other than corn might be grown in such a field. One might conduct a biological assay and plant some seed to see how it germinates. However, if one knows what herbicides were used it is possible to conduct the appropriate analyses and then make some recommendation as to the crops that might be planted. Pesticide residue analysis also becomes important when the possibility of contamination or damage exists. If some sensitive crop is damaged by drift or misapplication of a chemical, then it becomes necessary to determine what residues of chemical are on the affected plants before one can establish what actually happened. Agricultural crops which are exported and have to meet residue requirements imposed by the importing country should be sampled and analyzed prior to shipping.

The ability to analyze for pesticide residues also enables one to monitor the environment to determine the extent to which these chemicals are being distributed in areas other than agricultural areas where they were applied. It is also useful to be able to analyze for pesticide residues in intoxication cases. Normally, treatment has to be initiated before this information can be obtained. However, analysis of tissues can indicate the specific nature of the compound and indicate degree of exposure. This

information, if available, can be most useful in the treatment of intoxication cases.

It is thus quite evident that a competent analytical capability for pesticide residues is an integral part of a total program of pesticide management. This capability would more commonly be associated with those agencies regulating pesticide use either in agriculture or public health programs, as well as research establishments which are involved in the study of the behavior of these chemicals.

1. Analytical Procedures

The analysis of pesticide residues presents a special problem in analytical chemistry in that one is analyzing for very small quantities of a given chemical in the presence of large quantities of extraneous materials derived from the product to which the pesticide has been applied. To get around the problem of the large quantities of potentially contaminating materials, special extraction and cleanup procedures are utilized.

A. Extraction

Subsequent procedures require that the pesticide residue be in solution; thus, the initial step involves grinding or blending the sample with a solvent which will dissolve the pesticide. The analyst must be aware of the manner in which the pesticide is bound in the sample. On occasion it may be necessary to pretreat the sample to release the pesticide; otherwise, it will not be dissolved in the extracting solvent. No extraction procedure will remove 100% of the residue and in each situation a careful evaluation of the efficiency of extraction must be established. The analysts use the term "recovery" to indicate the efficiency of their procedures.

B. Cleanup

The analysis of pesticide residues would be simplified if the solvent extracted <u>only</u> the pesticide. Unfortunately, a considerable amount of the sample material is extracted along with the pesticide. To minimize interference in the subsequent quantitative measurements, as much of this extraneous material as possible must be removed. This is referred to as the "cleanup" step. This usually is accomplished by partitioning the extract against other solvents, or by adsorption on some solid adsorbent, such as alumina or florisil, followed by elution with appropriate solvents. Most of the interfering substances are either washed off the column prior to eluting the pesticide or retained on the adsorbent.

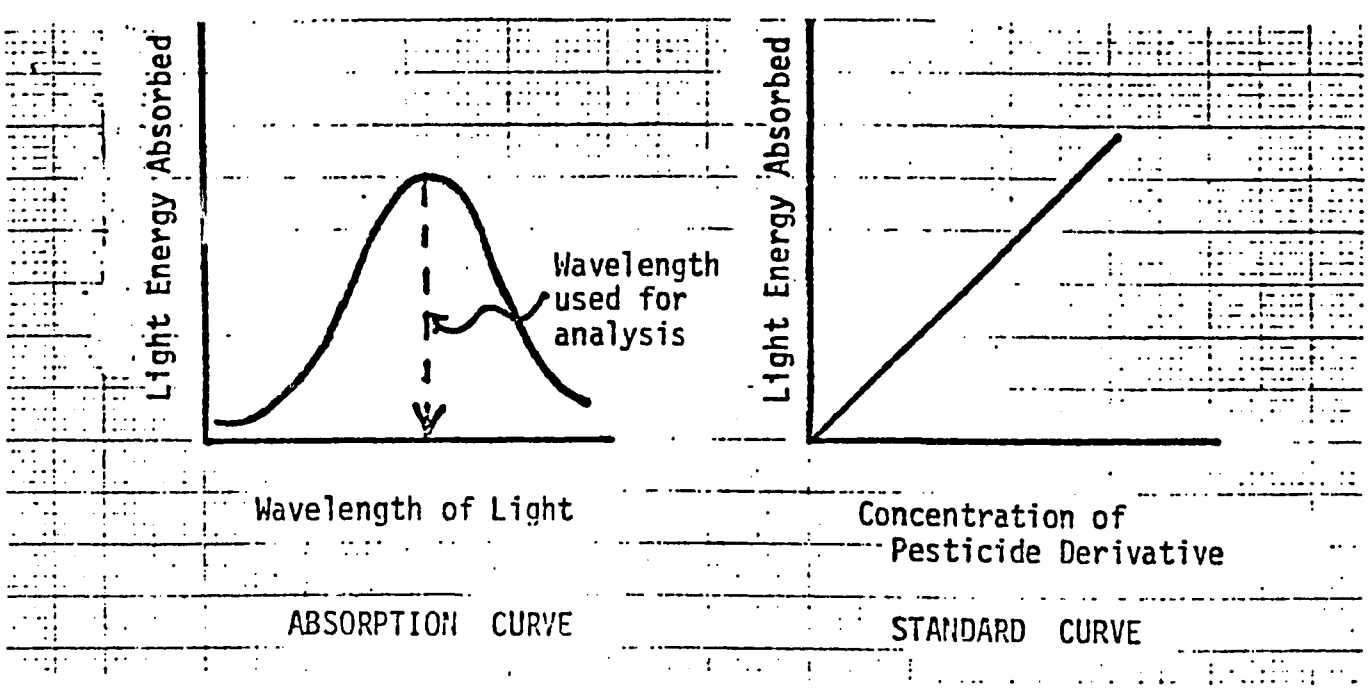
Cleanup procedures will differ from sample to sample. Water samples would require minimal treatment, while soil samples could present all kinds of problems because of the variety of components present. Thus the analysis of the same pesticide residue on a different product represents a completely new analytical problem since the extraction and cleanup procedures will always be different. At this stage the analyst would have a solution of the pesticide which would be, hopefully, relatively free from interfering compounds, and he would be in a position to make quantitative measurements.

C. Quantitative Measurements

Through the extraction and cleanup process the volumes used have been recorded and one will end up with a given volume of solution which would contain the pesticide extracted from a given mass of plant or animal tissue. The final step then in the residue analysis is to determine the concentration of pesticide in this solution. The procedure to be used must be sensitive since we are dealing with only small quantities of the pesticide compound, and selective because, even though considerable care is taken during the cleanup process, the final solution will still contain a certain amount of other compounds which could interfere with the analysis.

Gas chromatography has become by far the most important procedure used in the analysis of pesticide residues. Spectrophotometric procedures are also of some use and these two processes will be discussed.

1. Spectrophotometric or Colorimetric Analysis. Most pesticides are colorless in that they do not absorb light energy in the visible range. However, functional groups on some pesticide molecules can make it possible to convert the molecule into a colored derivative which does absorb light energy in the visible range. Using a spectrophotometer an absorption spectrum--light absorbed as a function of wavelength--is determined for the derivative. Using light of a wavelength of the maximum absorption of the derivative and solutions of known concentration, a standard curve is derived plotting light energy absorbed as a function of concentration.



The solution containing the pesticide residue is processed in the same manner as the standard samples, the colored derivative formed, and the absorption of the solution measured. Comparison of this value with the standard curve gives the concentration of pesticide in the extract. Con-

sideration of dilution factors and the mass of sample gives the residue level in the sample.

Spectrophotometric procedures are relatively simple and can be quite satisfactory. The primary disadvantages are limitations in sensitivity and problems from interference from extraneous sample material not removed by the cleanup process.

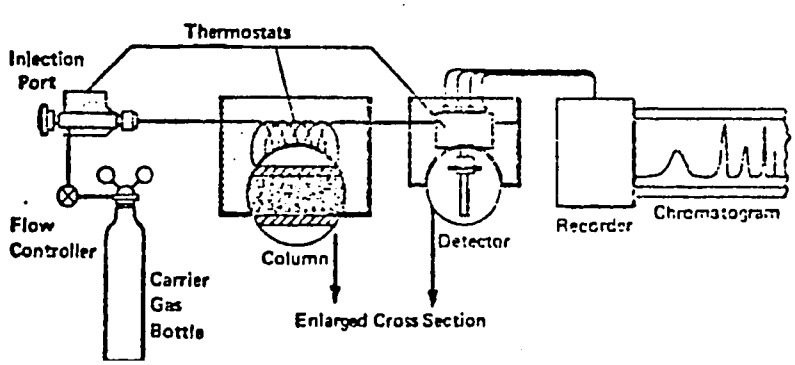
2. Chromatographic Procedures. Every chromatographic system consists of: (1) a stationary adsorbing phase--solid or liquid coated on a solid, and (2) a moving phase--liquid or gas. Samples are incorporated into the moving phase and the separation of compounds depends on differences in the way that compounds are distributed between the moving and stationary phases. The more strongly adsorbed would move the slowest.

a. Thin-Layer Chromatography. A thin film of the adsorbent (stationary phase) along with a binder is spread on a glass plate. The sample is applied as a small spot on one edge of the plate which is dipped into a liquid. The separation is accomplished by the liquid moving up the plate by capillary action. After the solvent front has moved a sufficient distance the plate is removed from the solvent, dried, and treated with reagents to make the compounds visible. The distance the compound travels relative to the solvent front is characteristic of the compound.

These procedures can provide good qualitative information as well as rough quantitative estimates. In a number of cases thin-layer chromatography provides an effective cleanup procedure.

b. Gas-Liquid Chromatography. This technique is by far the most effective and widely used procedure in pesticide residue analysis. The stationary phase is a high bioling liquid dispersed on a solid, and the moving phase, an inert gas. Variations in the liquid coating provide great flexibility in the types of separations which can be achieved.

The stationary liquid phase may be coated on the inside wall of a capillary tube or finely divided particles of an inert solid which is then packed into a column of about 3-6 mm in diameter. This column is housed in an oven whose temperature is controlled. The inlet end is connected to a cylinder containing the carrier gas and the outlet end to the detector. The sample is injected through a septum on the inlet end and is detected as it emerges from the column, giving a symmetrical peak on the recorder. For a given adsorbent system and temperature, the time for the compound to emerge (retention time) is characteristic of the compound and the area or height of the peak is proportional to the concentration.



The unusual effectiveness of this method depends on the sensitive detectors which respond to the compounds as they move off the column. The detectors are calibrated with solutions of known concentration and the level of pesticide in an unknown extract determined by reference to the calibration curve.

The flame ionization detector is simply a small hydrogen flame through which the sample passes after emerging from the column. The hot flame produces ions, generating a small current which is amplified and recorded on a strip chart recorder. By contrast with an electron capture (EC) detector, a radioactive element ^{3}H or ^{65}Ni is used to generate a current. Electrons from the radioactive element interact with the carrier gas producing more free electrons which provide the current. This detector responds to compounds emerging from the column which can absorb electrons and consequently reduce the current.

Characteristics of these two detectors are:

	Responds to	Detection Limits - g	Comments
Flame ionization	Carbon compounds	10^{-9} - 10^{-10}	Relatively trouble-free, not selective
Electroncapture	Compounds which absorb electrons, chlorine-containing compounds, aromatics	10^{-11}- 10^{-12}	Improved selectivity, very sensitive, difficult to operate

Two other detectors which find use in pesticide residue analysis are the microcoulometric detector which is specific for chlorine-containing compounds, and the flame photometric detector which is specific for phosphorus- or sulfur-containing compounds. With the microcoulometric detector the compounds emerging from the column are burned in a furnace; chlorine-containing compounds produce hydrogen chloride which is determined in an electrochemical cell sensitive to chloride ion. A hydrogen flame is used in the flame photometric detector to excite compounds moving off the column. In contrast to the flame ionization detector, it is the light emitted which is measured rather than the current produced. The light emergy is measured by a photomultiplier system and filters are used to select wavelengths specific for phosphorus or sulfur. Both detectors are sensitive in the nanogram range.

It takes a considerable amount of experience with a gas chromatograph to be able to obtain reliable information with any consistency. Both column performance and detector response are influenced in a complex manner by operating variables. Continuing maintenance of the electronic components of both the detecting system and the associated recorder is also needed for optimum performance.

D. Sampling and Sample Integrity

The most refined analytical procedures might be used and the most precise analytical information obtained; however, unless the sampling

procedures are adequate and the sample handled in a correct manner, this analytical information will be of little use. First, it is necessary to take a sample which will be representative of the material to be analyzed. And, second, once a sample has been obtained it is essential that it be handled in such manner that the sample does not deteriorate. For example, it has become well known that water samples taken in plastic bottles can give very erroneous results because the chemicals in the samples can bind to the plastic container; as a consequence the chemical would not be detected. Tissue samples must be frozen to eliminate any possible metabolic breakdown, and even under these conditions it has been demonstrated that there is some potential for the conversion of a pesticide into some other form.

When analyzing for pesticide residues it is always essential to analyze an untreated control to establish the type of interference that a particular sample will provide. This raises the problem of analyzing for pesticides in the environment. This presents somewhat of a different problem in that a control sample is not available, and thus to establish the presence of a particular pesticide residue in such a sample requires more rigorous procedures than the analysis of some product for pesticide residue when it is known that the pesticide has been used on that product. It is necessary to use more unequivocal procedures to establish the identity of the components in the environmental sample, and one has to use other techniques which will supplement the information obtained by gas chromatography.

E. Effectiveness of Analytical Procedures

The development of analytical procedures for pesticide residues has been most rapid, and with the introduction of gas chromatography and the development of very sensitive detecting systems, highly sensitive procedures are available for most of the pesticides currently in use. An indication of the capabilities of these procedures is summarized in the accompanying table where the sensitivity of these procedures is given for a number of rather common pesticide compounds. It must be emphasized that this area of analysis is somewhat specialized and requires competent technical personnel who understand the chemistry of the procedures which are being used, as well as the capabilities and limitations of the instrumentation which is being used in the analytical procedures.

Some Detection Levels for Pesticides in Different Samples

Pesticide	Detection Level*(ppb)	Analytical Procedure	Sample
DDT	10	GC. Electron capture	Adipose tissue
	0.2	"	Water
Endrin	20	"	Adipose tissue
	0.2	"	Water
Malathion	10	GC. Flame photometric	Fruits, vegetables
	1.4	"	Water
Ethyl parathion	10	"	Fruits, vegetables
	1.0	"	Water
Carbaryl	100-200	Spectrophotometric	Fruit, grain, hay
PCP	10	GC. Electron capture	Blood serum
2,4-D acid and ester	0.2	"	Citrus, water
	100	GC. Microcoulometric	Grass, milk
Simazine	50-100	Spectrophotometric	Fruit, vegetables
	10	"	Water
Paraquat	10	"	Potatoes
	50	"	Milk, meat

* These values are meant to give an indication of the lower level of sensitivity. This value could be increased if the sample gave considerable interference, or decreased if very special precautions were followed.

CHEMODYNAMICS

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Introduction

In the past quarter century man has introduced a variety of chemicals for the protection of his crops and health and to increase the comfort of his environment. These chemicals represent various classes of compounds and are used as pesticides, drugs, surfactants, and for a variety of other purposes. Recently, fears of environmental contamination from certain stable compounds used as pesticides have led to restricting their uses. It is true that pesticide residues have been found widely distributed in crops, soils, water, birds, fish, and air near the places of use. The understanding of how this distribution occurs and the fate of the chemical in relation to exposure of man is of importance in providing knowledge of how to use chemicals more safely.

Studies have provided an understanding of the emerging field of "chemodynamics" which demonstrates the relation of physico-chemical principles to the behavior and fate of chemicals in the environment. While the majority of the examples used deal primarily with agricultural chemicals (pesticides), the same principles apply equally to other similar organic compounds. Indeed, one of the benefits accruing from pesticide research is the development of knowledge of "chemodynamics" and toxicology that is applicable to all organic pollutants.

Basic to chemodynamics are the questions: (1) What are the natures and properties of the compounds under consideration? (2) What is the manner in which the properties of the compound and of the environment interact to influence the fate and behavior of the chemical? (3) To what extent does this determine the amount of the chemical to which man and organisms are exposed? These are the main features on which the present account of chemical research will be based.

Chemicals used as pesticides represent a wide variety of compounds. They are grouped according to the purpose for which they are used, e.g., insecticides for insect and mite control, herbicides for weed control, and fungicides for fungus control. Among the characteristics of the pesticides are that they are generally low molecular weight organic compounds and usually have limited water solubility; however, some inorganic compounds and organometallics also are used as pesticides as well.

In order to answer the question as to what happens to a chemical when it is introduced into the environment one must have an understanding

of the nature of the environment itself. The fundamental phases of the environment are: land (lithosphere), water (hydrosphere), air (atmosphere), and biota (biosphere). A rough estimate of the masses of the various phases yields the following:

(1) atmosphere 5.3×10^{18} kg

(2) soil to six-inch depth 1.1×10^{17} kg

(3) water 1.3×10^{21} kg

(4) animals 2.0×10^{13} kg

(5) plants 1.1×10^{15} kg

When a chemical is released into the environment it will be distributed (partitioned) between the various phases with the concentration in any phase being a function of the properties of both the chemical and the phase (Figure 1). Applying the simple law of Boltzmann distribution to this complex system we have the following equation:

$$N_{ij} = N_o e^{-\varepsilon_{ij}/k\,T}$$

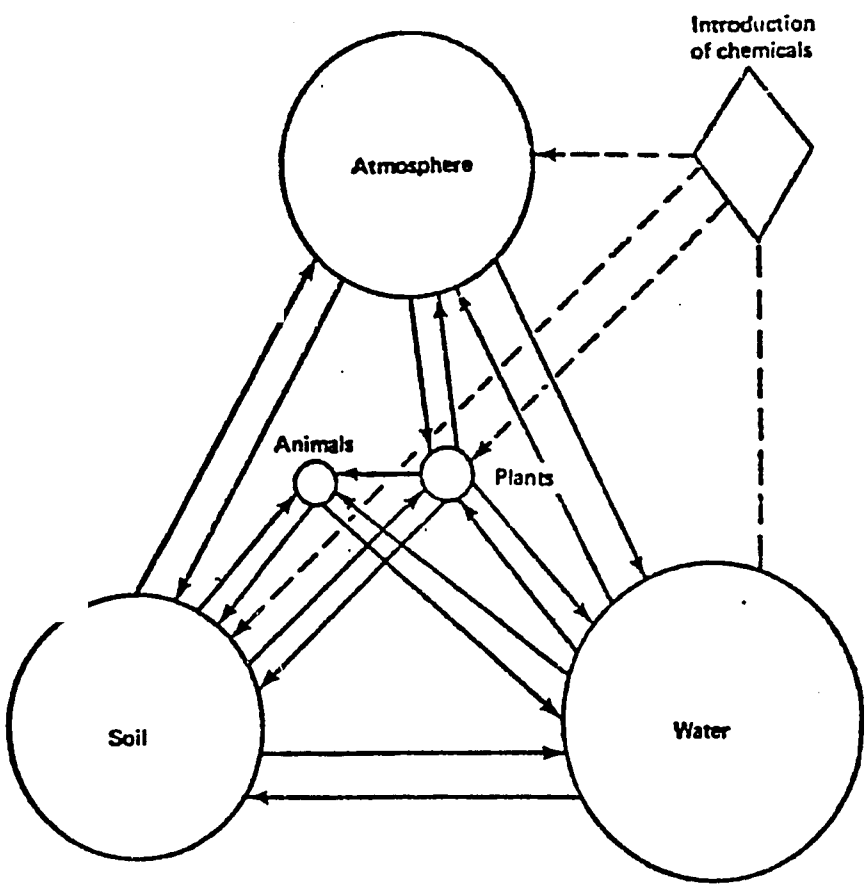
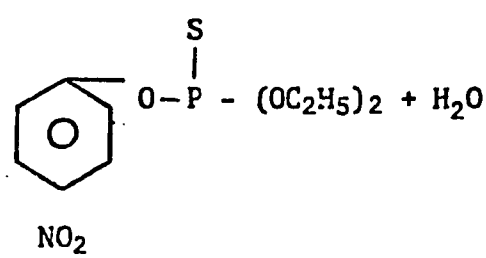


Figure 1. Schematic representation of the distribution of a chemical in various phases of the environment.

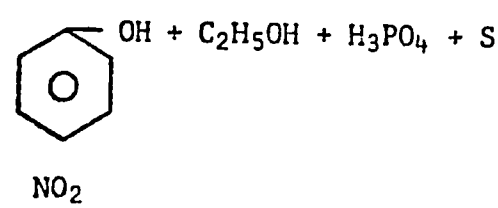
If we assume that $N_{ij} = N_{ji}$, $N_{ij} = 0$ when $i = j$ and $N_0 = N_1 + N_2 + N_3 + N_4 + N_5$, where N_0 is the number of molecules of the chemical initially introduced and $N_1 \ldots N_5$ are the number of molecules in respective phases of the environment. In the above equation ϵ represents the energy barrier between two phases, k represents the Boltzmann constant, and T represents the absolute temperature. To understand the behavior of a chemical in the above five components one must have a detailed knowledge of the physical and chemical properties of the chemical. In this chapter we shall try to discuss the principles governing the behavior of a chemical in atmosphere, water, soil, and biota. The decomposition of chemicals via various mechanisms will also be covered. While some abstract mathematics and chemistry are used in the study of this subject, the findings are of great practical importance as we will try to demonstrate. By application of the principles developed in chemodynamics, we can make more intelligent selections of the pesticide to use, develop methods for application that save money, and avoid some of the more serious residue problems.

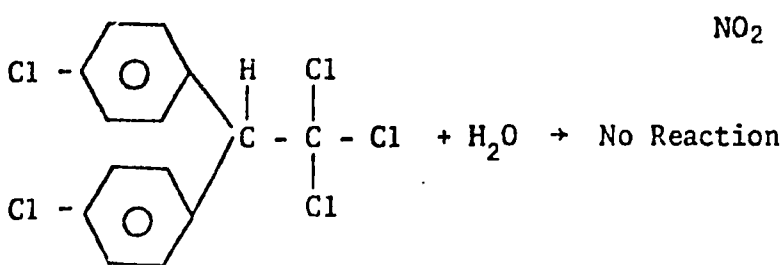
The basic information that is necessary to accomplish these things is data on properties of the chemical including such things as solubility in different solvents and at different temperatures, how readily does it vaporize, and how does it react with soil, plant and insect surfaces. The composition and structure of the chemical also tells us what type of reactions it is likely to undergo, and hence, to some extent how persistent the chemical may be.

For example in soil, the chemical is exposed to the soil moisture (water). We know that chemicals of a certain structure and composition will react with water being degraded in the process while chemicals of other structure do not react. This can be illustrated by the reaction of an organophosphate (parathion) with water in contrast to the inertness of DDT toward water.



Parathion





The same type of information about the chemical can assist in development of formulations to achieve the safest and most effective results with a particular chemical. Much of this information may be acquired through experience with a chemical in the field, but this takes a good deal of time and is costly. Fortunately, from some rather simple laboratory studies we are able to obtain a good deal of the information we need on a particular chemical, and use that as guidelines for more effective use.

Basics of Chemodynamics

All of the research to obtain this information requires a background of chemistry, but it does not take a chemist to understand the basic principles and apply them. The fundamentals are fairly simple and logical. These principles can be summarized very briefly by the following statements:

1. The behavior, biological effects, and persistence of a chemical result from the interaction of that chemical with the biota or some element of the environment.

2. The type and extent of the interactions depend in part on the measurable properties of the chemical.

3. Most of the nonmetabolic interactions of the chemical are to varying degrees reversible.

4. Knowing something of the nature of the interactions and the properties of the chemicals, one can predict to a first approximation the behavior and biological effects of a chemical.

To illustrate the application of these principles, let's take a chemical such as parathion used under semitropical conditions. Even without the benefit of field experience with this chemical, from properties that could be determined in the laboratory, we would predict:

1. Its adsorption by, and interaction with, soil, plant leaves, and animal life.

2. Breakdown of the chemical by hydrolysis and photochemical reactions resulting in a reduced period of control.

3. Vaporization of the chemical with loss of activity.

4. Need for repeated application to maintain insect control.

5. Fairly wide low level environmental distribution, but probably sufficient to cause the development of resistance in some nontarget insects.

These predictions are largely "negative" from the standpoint of economic pest control so that the question arises as to whether or not anything can be done about it. From the base of this information, it would then be possible to devise formulations and methods of use to achieve more effective and safe use of the chemical.

Importance of Chemical Properties

Let us now turn to a brief examination of some of the factors in the behavior of pesticides as we now use them. We recognize that each chemical is unique in that each has a set of particular chemical and biological properties different from any other chemical. It should be added, however, that these properties tend to follow patterns which make predictions possible. Certain of these properties are of value in understanding the chemodynamics of the compound and predicting its behavior. Some of these properties are easily measured in the laboratory and are most helpful in assessing the strengths and weaknesses of that chemical as a pesticide. For example, the solubility of a chemical is particularly important. Knowing the solubility can indicate how the substance should be formulated for application, whether as an emulsifiable concentrate, wettable powder, or in some other manner.

The solubility in water, if measured at several temperatures, is very useful in telling us whether the chemical will be strongly adsorbed by soil and other solid material, thus reducing its effectiveness or prolonging its persistence. Similarly, a knowledge of the solubility of a chemical in oil or other solvents as compared to water (actually partition coefficient) can tell us whether or not it is likely to accumulate as a residue in plant and animal.

The tendency of a chemical to volatilize or turn to a vapor is important, particularly where temperatures tend toward the warm side such as in the tropics. Vaporization means a loss of deposit for control of the particular pests, and also means considerable contamination of the air. The contamination results in exposure of animals and humans which is undesirable.

Other properties that are of interest and importance in providing guidelines as to how to more effectively use the chemical, include the type of reactions the chemical will undergo, and adsorption by soil or binding by constituents in the plant or animal. How knowledge of these properties may have practical application will be illustrated in the sections on adsorption, leaching, vapor behavior and breakdown.

Adsorption

When a pesticide is sprayed on a field, by far the greater proportion of it settles onto the plant leaves and the soil. Experiments have shown that the bulk of the chemical ultimately reaches the soil. Both the plant leaves and the soil present a solid surface to the chemical. The strength of this interaction (adsorption) depends a great deal on the properties of both the chemical and the surface that it encounters. For example, soil is made up of organic matter, as well as clay, sand, and silt particles. All of these are solid surfaces, but the organic matter of soil is found to adsorb much more chemical per unit weight than does the other constituents of the soil.

The amount of chemical adsorbed or bound by any one of the different surfaces mentioned varies depending on the chemical involved. To a first

approximation, one may say that the lower the water solubility of the chemical, the larger the amount that will be adsorbed. However, closer examination of the adsorption phenomenon shows it to be more complex than this. A better relationship as to the amount of chemical bound and the strength with which it is adsorbed is to be found in the quantity called "heat of solution." This can be illustrated in the following table of data which reports both the "latent heat" of solution (ΔH) and percent of available chemical adsorbed from laboratory experiments.

Chemical	ΔH	% Adsorbed
DDT	13.	>92
Dichlorbenil	2.8	48
CIPC	4.9	50
Monuron	6.0	64
DCPA	12.4	88
Dicamba	1.9	<40

This is a quantity that is calculated from the solubility at several temperatures, and once determined, permits estimates of the strength of binding and hence the susceptibility of the chemical to leaching and breakdown.

There are times when advantage can be taken of adsorption to extend the effective life of a pesticide or conversely to reduce the residual toxicity. An example of this latter case is where carbon or charcoal is used as an antidote for residues or poisoning.

Adsorption is a very important phenomenon in the use of pesticides. As indicated, much of the pesticide is adsorbed by plant or soil surfaces, and this can modify the activity. Additionally, adsorption regulates the leaching or movement of the compound by water and its loss from the soil by vaporization. There is an indication also that adsorption plays a role in the rate at which the chemical breaks down. That is, the more strongly adsorbed the material, the slower the initial rate of breakdown.

It is important to understand that the adsorption or binding of a chemical by a solid surface is a process that goes both ways, that is, it is a reversible process. It is because of this reversibility that most chemicals will leach, at least to some extent, as the water moves through the soil profile. If, for example, it is a chemical that is very weakly bound to the soil, rainfall may carry it quite deep into the soil. On the other hand, with a chemical that is strongly bound by all of the soil constituents, such as DDT, the chemical will be carried into the soil only for a short distance even by large quantities of water.

Leaching

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 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.

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 by 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 pesticides 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.

The following table showing the leaching of certain chemicals of different physical properties illustrates these points.

Chemical	Soil Type	Inches of H_2O	Depth of Maximum Concentration (inche
Trichlorobizoic acid	Loam	3	12.0
Monuron	Loam	3	2.0
	Clay	3	1.75
Simazine	Loam	12	1.0

Volatility

Somewhat earlier we mentioned the matter of vaporization or volatilization of pesticides. This is the tendency of the chemical to change from a solid or a liquid to a gaseous state. In certain instances, this tendency is advantageous such as in the case of the use of propoxur for control of mosquitoes in houses, or in use of space fumigants. On the other hand, where one may want a residual deposit of a chemical for pest control, vaporization can result in substantial losses, thus reducing the length of the control period and the effectiveness of the treatment. Where vaporization is a problem, as regards to control, modification of formulation or the use of additives can often reduce the rate of loss.

Almost all known substances have a tendency to vaporize. With the organic pesticides one finds a wide variation in the tendency with some compounds having relatively high vapor pressures compared to others. In general, the rate of vaporization increases as the temperature increases,

though humidity and other factors, e.g., adsorption, may modify the rate from the theoretical possible.

Breakdown

One of the important considerations of the 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 of the organic pesticides break down under the influence of the various biological and physical forces in the environment. For some compounds, the degradation by biological means, that is metabolism of plants and microorganisms is the most important. Other compounds break down through normal chemical reactions, examples of which include the hydrolysis of parathion by the moisture in soil. The rate at which a chemical will break down or be metabolized is dependent in part upon the nature of the chemical, the reactions that it undergoes, the conditions such as temperature and moisture, and, of course, the initial amount or concentration of the chemical. For example, while parathion breaks down very rapidly in soil at normal rates of usage, persistence of the chemical is much prolonged where excessive amounts are placed in the soil.

A mechanism of break down of pesticides, the importance of which we are now only beginning to appreciate, is that of photochemical reactions. Probably one of the reasons for the relatively short residual life of parathion is the fact that it is decomposed by the rays of sunlight. This reaction undoubtedly occurs on the plant leaf as well as after the parathion has vaporized into the atmosphere. Again, a practical application of such knowledge is that we can design formulations to reduce photochemical degradation.

Summary

In the course of these considerations, a number of factors relating to how chemicals behave in the environment have been mentioned and noted that it is possible to modify some of this behavior by a proper formulation or application technique. If the information is properly utilized it can result in more effective pest control at a lower cost, avoid some of the more serious residue problems, and prevent unnecessary human exposure. Much of the data required to do this can be obtained by rather simple and quickly performed laboratory studies. Though these may not give the final and most precise answer, they can be very important in developing guidelines and practices of better pesticide management. Even rough approximations of the values of certain of these parameters can be useful in guiding selection, formulation, and use of chemicals. The final tabulation provides chemodynamic "indices" of a few commonly used pesticides which may be of value in handling and use.

COMPARATIVE ENVIRONMENTAL BEHAVIOR OF PESTICIDES IN SOIL.[1]

Compound	Vaporization[2] index (from soil)	Leaching[3] index
Herbicides		
Alachlor	3.0	1.0-2.0
Propanil	2.0	1.0-2.0
Trifluralin	2.0	1.0-2.0
Dalapon-Na	1.0	4.0
MCPA (acid)	1.0	2.0
2,4-D (acid)	1.0	2.0
2,4,5-T (acid)	1.0	2.0
Insecticides		
Carbaryl	3.0-4.0	2.0
Malathion	2.0	2.0-3.0
Naled	4.0	3.0
Dimethoate	2.0	2.0-3.0
Fenthion	2.0	2.0
Diazinon	3,0	2.0
Ethion	1.0-2.0	1.0-2.0
Oxydemeton-methyl	3.0	3.0-4.0
Azinophosmethyl	-	1.0-2.0
Phosphamidon	2.0-3.0	3.0-4.0
Mevinphos	3.0-4.0	3.0-4.0
Methyl parathion	4.0	2.0
Parathion	3.0	2.0
DDT	1.0	1.0
BHC	3.0	1.0
Chlordane	2.0	1.0
Heptachlor	3.0	1.0
Toxaphene	4.0	1.0
Aldrin	1.0	1.0
Dieldrin	1.0	1.0
Endrin	1.0	1.0
Fungicides		
Captan	2.0	1.0
Benomyl	3.0	2.0-3.0
Zineb	1.0	2.0
Maneb	1.0	2.0
Mancozeb	1.0	1.0

[1] Estimated from best available information for loam soil at 25°C under annual rainfall of 150 cm.

[2] A vaporization index number of 1 = vapor loss of less than 0.1 kg/ha/year, 2 = from 0.2 to 3.0 kg/ha/year or more, 3 = 3.5 to 6.5 kg/ha/year or more, and 4 = 7 to 14 kg/ha/year or more.

[3] A leaching index number indicates the approximate number of centimeters moved through the soil profile with an annual rainfall of 150 cm; thus, an index of 1 = <10 cm, 2 = <20 cm, 3 = >35 cm, and 4 = >50 cm.

PESTICIDE APPLICATION

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INTRODUCTION

In the past two decades pesticides have emerged as an important tool in both agricultural production and public-health programs. Over one billion pounds of active pesticides were used in the United States in 1971. Herbicide applications have increased most rapidly, with farmer use increasing twofold from 1966 to 1971. In 1971 farmers used 228 million pounds of herbicides, 170 million pounds of insecticides, and 41 million pounds of fungicides.

Considering the worldwide shortage of both energy and food it is imperative that the efficiency of food production be increased. I believe that sound pest-management programs will be a major factor in increasing future food production. As an engineer I would like to point out that technology of application is a key link in efficient utilization of pesticides.

This paper discusses some of the principles of pesticide application, with the major goal of maximizing effectiveness and minimizing hazards. In general, techniques that may improve deposition of pesticide on the target will also reduce hazards.

Worker Safety in Handling and Mixing

A. Pesticide Label - A basic rule for safe handling of pesticides is to know the product. One method of providing essential information to the user is through the label. All pesticide containers in the United States must have a label with certain standard information. To name a few, the label must contain the name of the product, the name and percentage of active ingredients, the directions for use, and certain signal words denoting the toxicity. Each product is classified into a given category of toxicity based upon the LD_{50} or LC_{50} of the formulated product. For instance, the words, "Danger," "Poison," and a skull-and-crossbones symbol must appear on all highly toxic materials; and a "Warning" appear on Category "2" materials, and "Caution" on Category "3" materials. During the past summer, I had an opportunity to visit and observe some pesticide use problems in a few developing countries. One problem was lack of labels. In many instances the farmer would supply a bottle, oil can, or other small container to be filled from a large 55-gal. drum at the pesticide distribution center. No label was generally available for the small containers. In this case it would be desirable to have suitable tag labels that could be wired or otherwise attached to the farmer's containers.

B. Mixing and Handling the Concentrate Chemical - One of the most hazardous operations for the pesticide applicator is during the transfer

and measurement of the concentrate chemical into the spray tank. If a highly toxic material is handled, the worker must use waterproof protective equipment such as gloves, boots, apron, respirator, and goggles. These items should be checked routinely for leaks or tears, and regularly cleaned. Two basic problems have been observed in the field. One, the operator may need further training on all modes of entry of the pesticide. For instance, the applicator may utilize a respirator while measuring concentrate liquid pesticides with bare hands and feet, not realizing that many toxic insecticides can be readily absorbed through the skin. Secondly, in addition to the training, suitable protective clothing must be available if he handles highly toxic materials.

In 1974, a joint study was conducted by the California Departments of Food and Agriculture and Health to determine the extent of illnesses due to pesticides in each of several occupational categories. Table 1 summarizes the results. The two highest categories of reported illnesses were ground applicators, accounting for 28% of the illnesses, and mixer-loaders, with 11% of the illnesses. These data, along with other field observations, were considered in developing a new set of pesticide-worker safety regulations. The purpose was to provide safe working conditions for pesticide applicators. The regulations cover a wide range of requirements as to minimum age, training, medical supervision, operational procedures, protective equipment, equipment modifications, etc. I will only briefly discuss the requirement for a closed mixing system.

By January, 1977, California regulations will require that a "Closed Mixing System" be utilized for handling Category 1 (and some Category 2) liquid pesticides. This regulation requires a system that can transfer the pesticide from its original container into a closed mixing tank without exposing any person to the pesticide. Fig. 1 through 4 illustrate some approaches to "closed mixing systems." Fig. 1 illustrates a bulk handling system that has been utilized by some aerial applicators. This type of system is suitable for areas where large quantities of a few chemicals are applied. In some areas bulk tanks of several thousand gallons are utilized. Fig. 2 illustrates a simple system developed by some California mosquito-abatement districts. The system consists of a simple closed gravity-flow system for transferring the chemical into a translucent vessel. This system could possibly be adapted for dispensing pesticides from large drums into smaller containers, appropriate for use by small farmers. Fig. 3 is a portable system developed by a commercial aircraft operator. This system has been refined to also rinse the pesticide container after it is empty. The unit is currently being field tested and may be commercially available in the near future. Fig. 4 illustrates a closed system for handling dry powders that was developed by Dr. G. Carman and R. L. Metcalf at the University of California, Riverside. This closed system was designed to handle prepackaged containers of toxic wettable powders.

Some new packaging techniques are under development that may offer a real improvement for handling and loading toxic pesticides into small knapsack sprayers. At present, several companies are working on water-soluble packages. For example, the pesticide could be prepackaged into the quantity required for a 3-gallon sprayer. The applicator could then drop the unit into the sprayer and be ready to spray without exposure to the concentrate

chemical. Another system that is very attractive is microencapsulated formulations. This system provides a solid inert film around each pesticide particle. Thus this formulation can substantially reduce the hazard of exposure of the applicator to the pesticide. Microencapsulated formulations of methyl parathion are now available commercially.

Although some of the above approaches are in the experimental stages, some new developments are already on the horizon. Some of the improvements in handling techniques should be particularly helpful in the tropics where it is difficult to wear waterproof clothing in the heat.

Principles of Selecting and Operating Ground Sprayer Equipment

A. Protective Clothing and Equipment - The type of application equipment and toxicity of the chemical largely dictates the type of protective equipment required. With knapsack blower sprayers, a very fine-drop spectrum is produced and emitted into the air. Thus, if the material is highly toxic, the applicator should be fully protected with waterproof trousers, coat, hat, gloves, and respirator. I realize there are some real problems in using this equipment in the heat. It may then be necessary to use a less toxic pesticide or a less toxic formulation, such as a microencapsulated formulation as mentioned earlier. Another approach is to apply it only in morning or evening, when protective clothing can be worn. With compressed-air knapsack sprayers the inhalation problem may not be serious, making a gauze-type mask sufficient. If the operator walks through the sprayed vegetation, however, dermal exposure would probably be high and waterproof clothing would be essential. Some ventilation for worker comfort may be obtained by using a split-type waterproof apron.

B. Nozzle Selection - The nozzles perform three important functions: 1) meter the liquid; 2) atomize the liquid; and 3) distribute the material over a given area. Nozzle selection should be based on all three of the above functions. Nozzles must be selected of proper size to put on the quantity desired. The other points to consider are the droplet size desired and type, uniformity, and width of spray pattern. Some of the different patterns available are hollow-cone, solid-cone, and flat-fan patterns. Basically, the degree of atomization is very important to efficiency and drift hazards. The major factors affecting particle size are nozzle type, size of nozzle, and spray pressure. Generally, an increase in fan angle, a decrease in orifice size, and an increase in spray pressure result in a decrease in particle size. Gravity-flow flooding nozzles can be operated with a head of only two feet, or less than one pound per square inch. This produces a very large drop size and a minimum of drift. We have used this type of nozzle successfully for application of 2,4-D for morning glory control in vineyards. The gravity-flow system can be used in connection with a knapsack sprayer. In this case the tank can be easily modified to provide a constant head by means of an appropriate air-inlet tube extending to the bottom of the tank. The system operates without an air pump since the liquid merely flows by gravity, with a constant head maintained between the bottom of the air inlet and the nozzle height.

The pattern or uniformity of distribution is another important aspect in nozzle selection and operation. Generally, flat-fan nozzles provide a

nearly ideal triangular or trapezoidal pattern that can be readily matched or overlapped to obtain a nearly uniform distribution pattern. The optimum overlap will depend on the type of nozzle and operating pressure. For a given set of conditions there is an optimum nozzle spacing and boom height. One way of determining the optimum height is to put a pair of nozzles on a test stand with a "V"-trough table and graduated cylinders to measure the distribution pattern.

An important aspect of application that cannot be overemphasized is the need to calibrate the system to deliver the desired amount of chemical. Since the calibration may change as nozzles become worn, it should be checked at frequent intervals. I will not list the formulas, but each spray supervisor should know how to check the flow rate and the final application rate per acre for his equipment. Many materials have extremely critical tolerance levels: harming the crop if the application rate is too high, and ineffective if too low.

Principles of Aircraft Spray Techniques and Drift Hazards

Agricultural aircraft are basic to many pest-control programs in agriculture, forestry, and public health. The United States and Russia are by far the largest users of agricultural aircraft. Available statistics show there are 6100 agricultural aircraft in the United States, treating approximately 42 million hectares per year. Russia has about 7000 aircraft, treating approximately 75 million hectares per year. Statistics collected by the International Agricultural Aviation Center in the Hague, Netherlands, indicates that aircraft are used extensively in some 61 countries. Although many benefits are attributed to aircraft, some problems have arisen. One basic problem is the drift or movement of spray out of the target area. For example, drift of minute quantities of certain pesticides may cause serious injury to nearby people, crops, animals, or wildlife, or may contaminate edible food supplies. Some techniques to minimize drift hazards while maintaining efficacy of treatment are as follows.

A. Nozzle Selection and New Developments - Control of particle size is one of the most important factors in controlling pesticide drift. The size and density of particle determines the terminal velocity or settling rate in still air. Table 2 illustrates the terminal velocity and theoretical drift distance for a wide range of particle sizes. The theoretical drift distance was based on a uniform wind velocity of 5 mph, a release height of 15 ft., and zero evaporation. Although assumptions are considerable, the values emphasize the importance of reducing the number of very fine particles. Unfortunately most conventional nozzles produce some particles less than 100 micrometers in diameter. Drift can be minimized by proper selection of nozzle type and orientation with respect to the airstream. A very low drift level can be achieved by using a simple orifice (with no core) and directing it backward with the airstream. At 100 miles/hr, this produces a VMD of approximately 900 micrometers and has been used satisfactorily for 10-gpa applications of translocated compounds such as 2,4-D. Another common nozzle for use with insecticide applications at 10 gpa is the D6-46 hollow-cone nozzle directed backward with the airstream. This nozzle produces a VMD of 450 micrometers. Another common nozzle for low-volume applications of insecticides is the D6-45 nozzle directed down.

In comparisons of drift fallout 1/2 mile downwind from aircraft applications, the D6 orifice gave only 1/30 as much drift as the D6-45 nozzle, and the D6-46 was about 1/3 as much as the D6-45.

Some new atomization concepts and developments may provide a major breakthrough in controlling spray drift. AmChem has developed a "Microfoil" atomizer that consists of an airfoil-shaped manifold with small tubes (0.013 inch I.D.) molded at 0.1-inch spacing along the trailing edge. The system produces a very uniform drop size of about 900 micrometers. The system is probably the best commercial system available for minimizing drift hazards. Unfortunately, it is useful only on helicopters or vehicles where the air-stream doesn't exceed 60 MPH. We are currently conducting research on some experimental units designed to produce a nearly uniform particle size of 250 micrometers. This particle size would be suitable for fixed-wing aircraft application speeds of 100 to 110 MPH. The device uses a small jet-stream principle along with a piezoelectric crystal oscillator.

B. Formulations - A number of spray adjuvants have been introduced as a possible means of altering the atomization process to reduce the number of fine particles. We have measured the drift with both fallout sheets and air samplers for applications with a polyvinyl polymer (Nalco-Trol) and a hydroxyethyl cellulose buffer system (Union Carbide). The air sampler data indicate the greatest differences in the systems. The Nalco-Trol adjuvant produced the lowest amount of material collected by air samplers 330 ft. to 1 mile downwind. The hydroxyethyl cellulose adjuvant also produced a lower amount of deposits on the air samplers than did a standard emulsion spray. All the above tests were with a simple jet nozzle directed backward for minimum drift. The drift residues on the fallout sheets, however, showed no significant differences over the range from 165 ft. to 1/4 mile downwind.

C. Micro-Weather Factors - Micro-meteorological parameters are probably one of the most important but least controllable factors affecting drift residues. The aircraft operator should recognize the important influence of two factors: 1) wind direction; and 2) atmospheric turbulence. Fortunately, wind direction can be easily measured, and it is obvious that drift will not occur upwind onto an adjoining field. The second factor of turbulence is difficult to measure, and it is likewise difficult to predict the effect of turbulent mixing on the downwind spray drift concentrations.

The smoke plume from an old tire is an excellent visual indicator of wind direction and is useful in estimating turbulence or particulate diffusion. In fact, the use of a smoke column is a standard procedure for aerial applicators applying 2,4-D in certain hazardous areas of California. For example, a smoke plume during normal lapse conditions will rise, mix vertically, and diffuse rapidly. During strong temperature inversion the smoke flattens out and may remain intact for several miles, indicating very stable conditions with minimum vertical mixing or dilution. The mixing or dilution of the spray-drift "cloud" follows a similar pattern.

However, in an effort to quantify important turbulence parameters, a number of variables were measured during a large number of spray drift tests. It was found that the stability ratio was closely correlated to the drift fallout patterns. The stability ratio can be calculated as

follows:

$$\text{Stability ratio} = \text{S.R.} = \frac{T_{32} - T_8}{V^2} \quad (27.8)$$

where T is air temperature in degrees F at elevations of 8 and 32 ft., and V is the mean wind velocity in miles/hr. at 16 ft. Thus, the temperature gradient and wind velocity can be combined into a single index to predict drift fallout residues. A typical range of stability conditions follows:

Atmospheric condition	Stability ratio
unstable	-1.7 to -0.1
neutral	-0.1 to 0.1
stable	0.1 to 1.2
very stable	1.2 to 7.0

The spray tests were made with a very low drift system utilizing D6 jets directed back. The fallout measurements at 660 ft. downwind indicate that residues were 13 times as much during very stable conditions (S.R. of 5.8) as during low-stability conditions (S.R. of 0.2). Total air burden followed the same trend. At 660 ft. downwind the very stable conditions produced about 4 times as much concentration in the air as did low-stability conditions.

In conclusion, some important considerations to minimize drift from aerial applications: 1) Select nozzles that produce a minimum of fine drops consistent with pest-control results; a simple orifice or jet directed back is ideal for minimum drift with chemicals that are translocated or systemic. 2) Some types of thickening agents will further reduce the pesticide concentration in the air although they may have little effect on fallout levels. 3) Avoid application of toxic materials during the very stable conditions associated with strong temperature inversions.

Table 1

REPORTS ON PESTICIDE-RELATED OCCUPATIONAL ILLNESS IN CALIFORNIA IN 1973

OCCUPATION	SYSTEMIC	SKIN	EYE/SKIN	EYE	TOTALS
TOTALS	665	452	33	324	1,474
Ground applicators	187	103	13	121	424
Mixer loader	121	19	3	22	165
Field worker	45	94	0	18	157
Nursery greenhouse	18	71	1	22	122
Formulating plant	41	15	2	5	63
Warehousing loading trucks	33	8	1	9	51
Gardener	14	16	2	34	66
Firefighting	41	0	0	1	42
Fumigation	52	13	1	5	71
Creosote application	1	24	2	9	36
Drift	10	5	0	11	26
Structural pest control	11	5	0	8	24
Flaggers	16	3	0	1	20
Cleaning and machine repair	10	6	1	5	22
Aerial application	10	0	1	3	14
Other	55	70	6	50	181

Table 2

Particle diameter, micrometers	Terminal velocity (sp. gr. = 1.0) ft/sec.	Horizontal drift dist. (released 15 ft. elevation, 5 MPH wind)	No. of drops based on 10 gal/AC., drops/in^2
10	0.01	11,000.	$1.15\ 10^7$
50	0.25	400.	92,195.
100	0.85	129.	11,524.
500	6.8	16.	92.
1,000	13.2	8.	11.

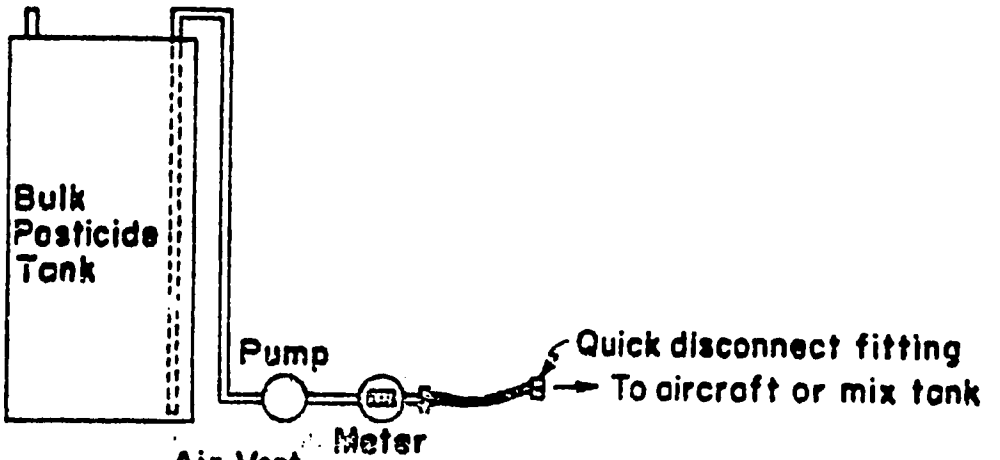

Fig. 1

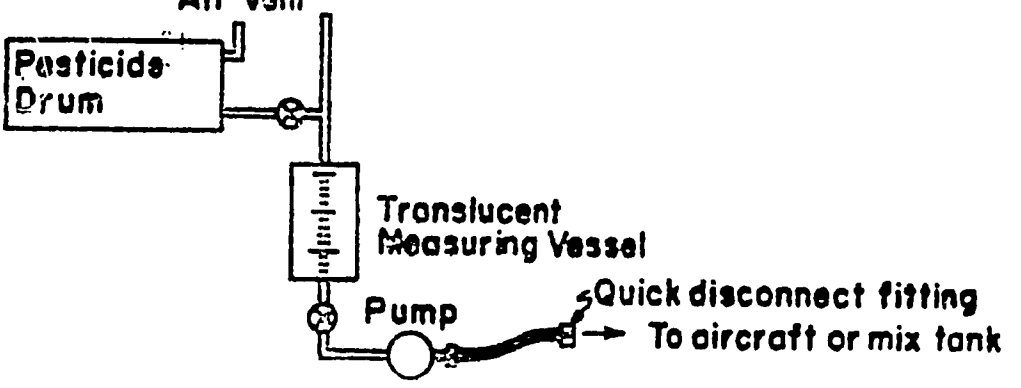

Fig. 2

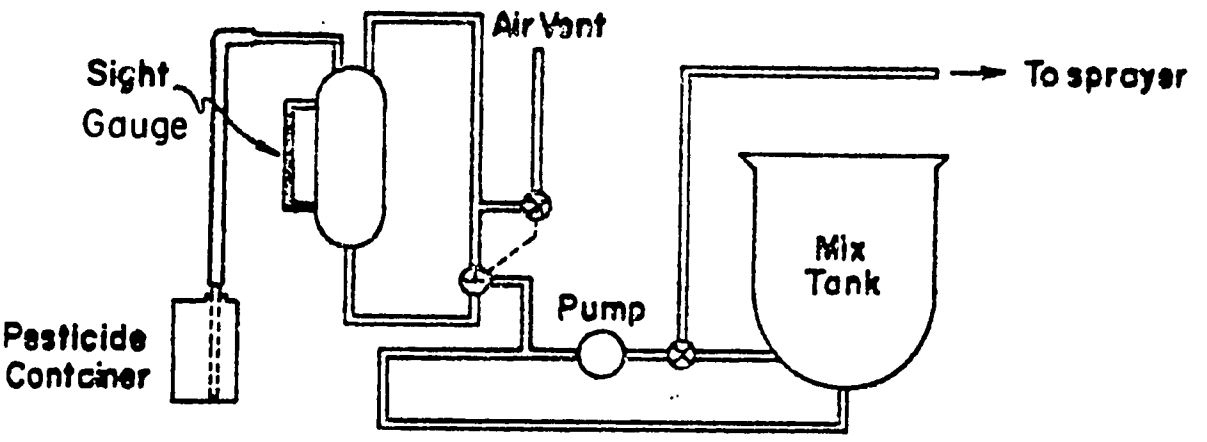

Fig. 3

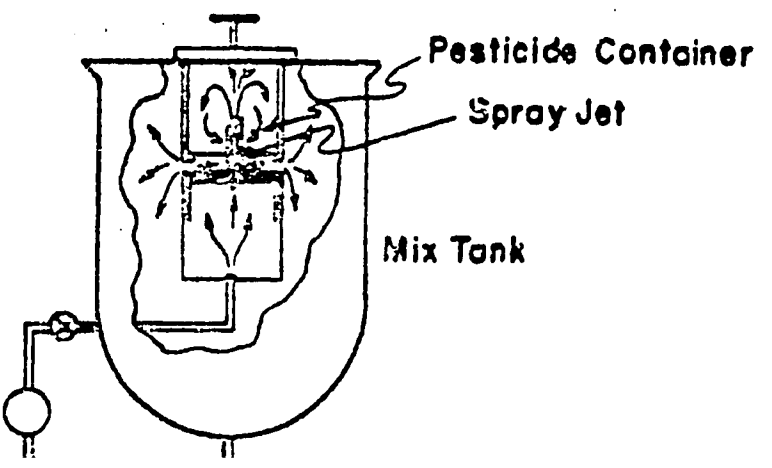

Fig. 4

FORMULATIONS OF PESTICIDES

FOR SAFER MORE EFFECTIVE PEST CONTROL

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Introduction

Over the past half century pesticides have become very important tools in agriculture and public health. Use of these chemicals for control of insects, weeds, fungi, and other pests has contributed greatly to increasing quantity and quality of food. Even more dramatic has been the control of such scourges as malaria and typhus through the use of pesticides. However, pesticides, particularly when used improperly may have undesirable side effects. Consequently, in the last few years, very substantial efforts have been directed toward finding non-chemical means of pest control. There have been developed promising leads for either non-chemical or minimum chemical use methods of pest management involving biological control, use of pheromones, attractants, hormones, and of course, application of a system of integrated pest management. Despite this however, there are many pest problems for which pesticides remain the only means of control. Consensus of opinion by many scientific groups that have studied the problem is that pesticides will remain the principal weapon of pest control for the foreseeable future.

If, then, pesticides are so important for the protection of our food supply and health, they deserve to be used in the safest and most effective manner. These chemicals employed as pesticides are highly sophisticated tools of technology with biological effects not limited to the target organism but may equally affect a wide variety of other organisms. Consequently, efforts to achieve safer, more efficient application and utilization of these chemicals are well worth the effort. Beyond this is the economic consideration where because of the increasing prices of pesticides and possible shortage of some, it becomes important to maximize the efficiency of use. It will be contended in this presentation that proper formulation will help to achieve both greater efficiency with the pesticides as well as greater human and environmental safety.

Types of Formulations

Few chemicals may be used directly as the technical product for pest control. 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. It has been estimated that in some instances as little as 10% of the chemical now applied to crop areas is all that is necessary

to control the pest if all of it could be targeted directly on the pests. Due to our inability to target the application directly on the pest and the various losses that occur, amounts of chemical to compensate must be used. For example, a factor entailing use of more chemical than the specific amount required to control pests, is the breakdown 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 a period of time.

Formulations of chemicals may be of various types, also some chemicals may be offered in more than one type of formulation. The formulation usually consists of a diluent such as a dust base or a solvent combined with other ingredients to afford 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. Some of the common types of formulations now in use are described below.

Dusts

Dusts are formulated for direct use and require no further dilution. The active ingredient content in dust usually varies from 1 to 10 percent, though higher percentages of active ingredient may at times be used. Because of their bulky nature, dusts are usually prepared locally from dust concentrates by diluting with an appropriate inert material such as attaclay, flour made of husks of nuts, or other materials. The inert ingredient must be selected not only for ease of application, but also compatibility with the pesticidal chemical.

For very obvious reasons dusts are very finely ground. They are easier to apply than the wettable powders or emulsions, usually utilizing much simpler equipment. Compared to some of the other types of formulation they are less apt to by phytotoxic in the case of the insecticides, but are highly susceptible to drift during application. Generally there is less toxic hazard through dermal exposure from dusts, but probably they are equally as hazardous as other formulations through inhalation. Dusts are readily removed from plant surfaces by wind and rain so that their residual life will be shorter than some of the other types of formulations.

Granulars

The formulation of pesticides into larger particles for direct application has been particularly well suited for application of pesticides to soil. They are usually prepared in concentrations similar to those used in dusts, that is from about 1% on up. Because of their size, the granular formulations of pesticides do not drift and do not stick to foliage. Like dusts, the granulars are formulated utilizing inert carriers such as one of th

clays, an appropriate binding agent, and pressed into the size particle desired. Granulars, of course, are unsuitable for treatment of foliage, and may have the additional disadvantage in some instances of having a lower biological activity because of adsorption on the clay. It is believed that substantial improvement in granular formulations, particularly for systemic insecticides, could be achieved by using sustained release formulations.

Wettable Powders

Wettable powders are essentially the same type of formulation as dusts, except that they contain a wetting agent. A wetting agent is for the purpose of dispersing the powder in water. The concentration of active ingredient of wettable powders will range from about 10 to 75%.

Wettable powders suspended in water will soon begin to settle out unless stirred or agitated.

Some of the physical properties of wettable powders which are important in application are: their uniformity of distribution, particle size, wettability and suspensibility. These must meet reasonable standards for ease of application and effective results.

Liquid Formulations

Liquid formulations, whether a water soluble derivative or emulsifiable concentrate, are designed for spray application with a suitable carrier liquid. In some instances the formulation is designed for very low volume (ultra low volume) application without further dilution. There are a variety of so called liquid formulations ranging from water soluble materials (amine salt of 2,4-D) to flowable formulations which are finely ground solids dispersed in a suitable liquid designed for spray application to emulsifiable concentrates (ethylparathion EC). Recently a number of variations of liquid formulations have been developed. Among one of the more interesting developments has been that of microencapsulated methylparathion in which the chemical is encapsulated in plastic beads. This formulation is designed for spray application. It has lower mammalian toxicity through skin absorption, as well as oral ingestion, and a longer residual life on the plant than the comparable emulsifiable concentrate.

Factors Influencing the Effectiveness of Pesticides

Before discussing some of the methods of improving the formulation and application of pesticides, it may be desirable to consider some of the factors that influence the effectiveness of chemicals. By understanding these factors it may be easier to design a formulation that would counteract the particular type of loss or losses that would tend to limit the effectiveness and/or increase the hazard of the chemical.

For purposes of this discussion, attention will be given primarily to the organic chemicals which make up the bulk of the pesticides used. Each

of these chemicals has a unique set of physical and chemical properties such as melting point, boiling point, vapor pressure, solubility, reaction rate, and tendency to adsorb on the surface of solids. Almost everyone has made the observation of the difference in rates of evaporation, of let us say, gasoline and lubricating oil. Gasoline evaporates very rapidly where the lubricating oil is very slow to evaporate. The difference in the rate of evaporation can be ascribed to differences in physical properties, i.e. the vapor pressure. Differences in some of the other physical properties are not so readily observed in common experience but are familiar to all chemists.

The environmental conditions, for example, temperature, moisture, sunlight, are important in how the chemical will behave. Returning again to everyday experience using the example of gasoline and lubricating oil, we know from observation that the gasoline will evaporate much more rapidly at high temperature than at low. This is also true of our pesticides, namely that as the temperature goes up, their rate of evaporation increases. Similarly, rate of loss goes up as the surface area increases. This can be illustrated by noting the difference in the evaporative rate loss between a quantity of water in an uncorked bottle and the same amount of water spread out over a large surface.

The loss of pesticides from plant surfaces washed off by rain is another factor that influences the effectiveness of pesticides. If, for example, an insecticide has been applied to a cotton crop and shortly thereafter, a hard rainfall occurs, much of the pesticide will be washed off the leaf. The consequence of this loss is that another application of the insecticide must be made in order to provide protection against the insect population. It might be said here that one of the objectives of formulating chemicals for regions where high rainfalls may occur should be to develop those formulations that would help to overcome washing off of the pesticide.

For the control of some pests, the chemical must be applied to the soil. In the soil, two distinctly different processes may occur, both of which can limit the effectiveness of the pesticide by reducing its persistence or reducing the concentration available for biological activity. The first of these processes is adsorption. This phenomenon involves the binding of the chemical to the surface of the soil constituents or other solid materials. Depending on how strong this binding is, the adsorption may substantially reduce the concentration of chemical available for controlling the pest. The other process is that of breakdown. The breakdown may be chemical, as for example in the hydrolysis of an organophosphate, or it may be microbiological in which case the bacteria and fungi of the soil metabolize the chemical reducing both its concentration and persistence. Table I attempts to summarize some of the environmental factors that influence or limit the effectiveness of pesticides.

Table I

Environmental Factors Influencing Effectiveness of Pesticides

1. Temperature - (height and variation)

2. Rainfall - (moisture supply)

3. Light - (intensity and quality)

4. Soil

Losses of the chemical, in terms of both concentration and persistence occur after application, but they also may occur during the application. By way of illustration, consider the spray application of an emulsifiable concentrate of a reasonably volatile chemical. During the spraying operation, the solution, or emulsion, is broken up into fine droplets that require a certain period of time to fall from the nozzle to the target plant or to the soil. If the droplet is very fine and the distance of fall excessive, evaporation may occur from the droplet. Also, note that the higher the temperature, the more rapid this evaporation may be.

There may also be a form of degradation occurring during and after the application. This occurs when the compound absorbs light energy from the sun rays and undergoes breakdown. Many of the organic chemicals used as pesticides are susceptible to this type of degradation. It can occur both during the application and on the surface of the leaf after the chemical has been applied. This, together with vaporization from the leaf and possible washoff can rapidly reduce the concentration of the pesticide on the plant or soil surface below the amount required to give adequate pest control. Table II is given to summarize these different factors.

Table II

Factors Limiting Effectiveness of Pesticide Application

1. Losses during application

2. Degradation

   Chemical
   Biological
   Photochemical

3. Vaporization

4. "Wash off" with water

5. Adsorption

6. Leaching (in soil)

Since it is now believed that evaporation can be quite an important source of loss of many of our pesticides, particularly in tropical regions, this

phenomenon needs to receive considerable attention in formulation. Table III attempts to illustrate some of the factors involved in vaporization to serve as a reminder of the importance of this route of loss.

Table III

Evaporation (Volatilization) of Chemical

1. All chemicals tend to vaporize

2. Temperature accelerates

$$\frac{dP}{dT} = \frac{\Delta H_v P}{RT^2}$$

3. The larger the area, the more evaporation

4. Below a certain size of droplet, the rate of evaporation increases

$$\frac{P_2}{P_1} = e^{\frac{2\gamma v}{r(RT)}}$$

Figure I is shown to emphasize point number 4 of Table III and serve as a reminder of the importance of controlling the drop size and the volatility of both the chemical and the carrier so as to minimize evaporative and drift losses during application.

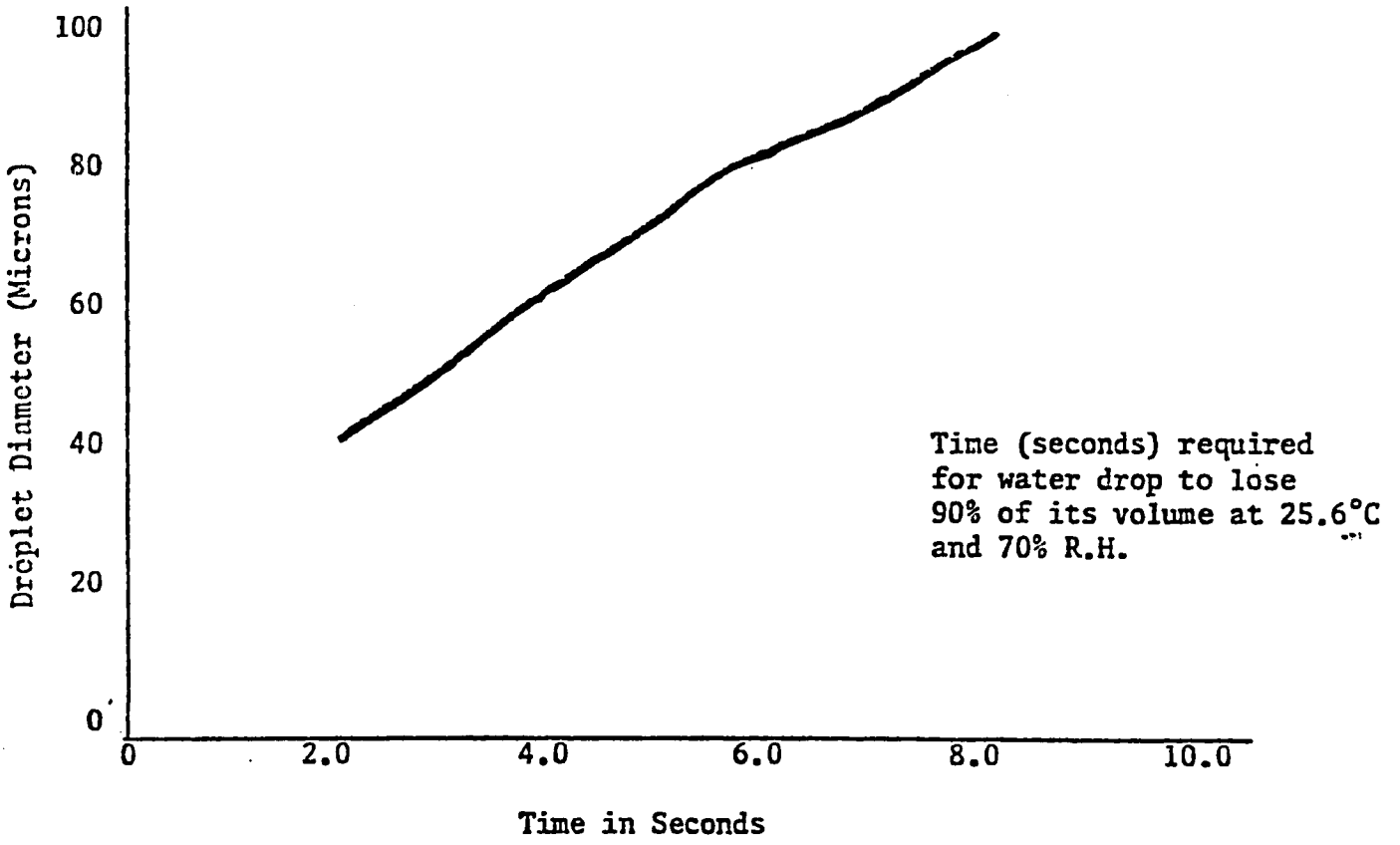
Considerations in Improving Formulation

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 was to ensure the chemical stability and shelf life of the formula and only then was consideration given to modifying the formulation to maximize the biological effectiveness. Only recently has more attention been given to developing formulations for 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 limit the effectiveness of pesticides. For example, as more was learned about drift occurring during application there was recognition for the need to not only improve application equipment, but also formulations to reduce drift. The addition of thickening agents to increase viscosity of the spray and the use of invert emulsions has gone a long way in reducing this problem with some chemicals.

Degradation is another factor that is important in limiting the effectiveness of a pesticide. The degradation as indicated earlier may be photochemical such as would occur on a leaf surface or chemical degradation as

Figure I

Evaporation vs. Drop Size



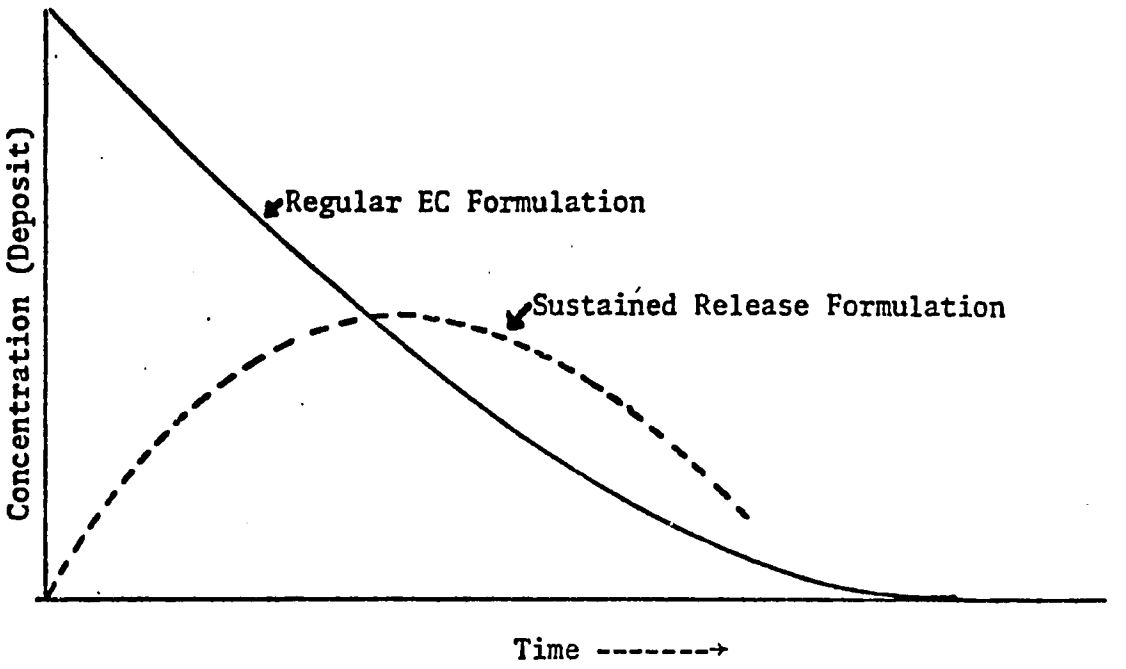
for example, hydrolysis or biodegradation as might occur in the soil. Degradation, of course, brings about a decrease in the concentration of the pesticide and when the concentration drops below the biological effective level, pest control ceases. There has been a rejection of persistent pesticides or those that do not degrade readily to those that break down more rapidly. To be sure, in order to protect the environment it is desirable to have chemicals that degrade, but we would like to slow down the degradation until the pest control has been achieved.

Various approaches have been used to reduce rate of degradation of chemicals. One approach for foliar applied chemicals has been to add an agent that screened out the shorter wavelengths of sunlight in order to protect against photochemical degradation. In cases of soil applied pesticides, the addition of a chemical that reduces microbiological attack has been successful in some cases. An even more successful approach has been the design of sustained release formulation in which the chemical is incorporated into a plastic or similar agent that protects it from attack by the release of the chemical over a period of time at a rate sufficient to give pest control. Figure II graphically depicts the difference between a regular emulsifiable

concentrate formulation and the sustained release formulation. The curves drawn in this figure represent the concentrations of the chemical at different time intervals.

Figure II

Illustration of Regular vs. Sustained Release Formulations



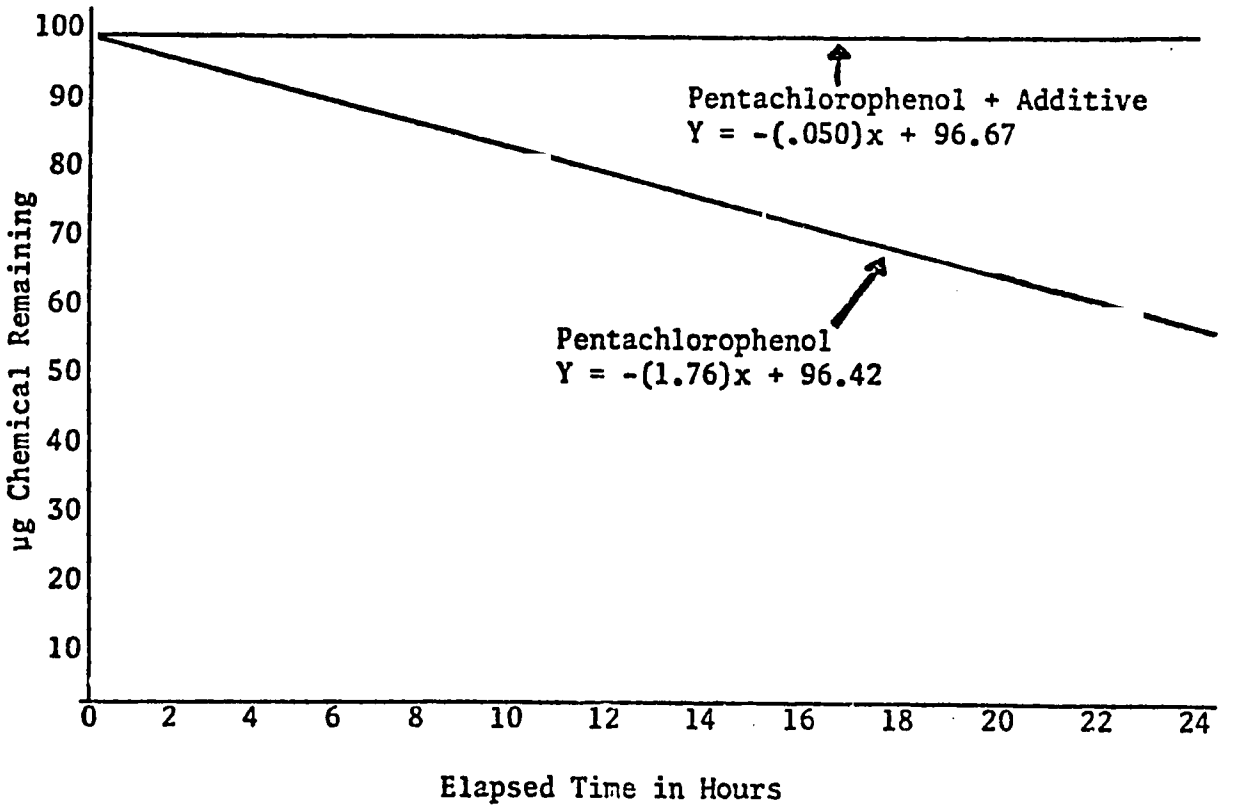
Another route of loss of chemicals is through vaporization or the change to gaseous form and escape from the treated area. Even though most of the pesticides used would be categorized by the organic chemist as being low in volatility, substantial vapor losses are experienced in field applications. The explanation for this is that there is a very thin film of chemical spread over a large area, and even though the percentage loss per square centimeter is low, substantial amounts are going to evaporate when spread out in such a film.

The vapor loss of a chemical can be reduced by formulating originally as a sustained release or microencapsulated product but this may not always be either desirable or feasible. Instead, it may be necessary to add an ingredient just prior to application that would tend to reduce the rate of vapor loss. Figure III is an illustration of what can be done in reduction of vapor loss with certain additives. The same additive is not necessarily suitable for all chemicals, but it does now appear that vapor controlling additives can be found for a number of chemicals.

Figure III

Effect of Additive on Volatility of Pentachlorophenol

Micrograms Remaining vs. Time in Hours



In an earlier section, the problem of "wash off" was indicated as another source of loss of pesticides from plant surfaces. Again, additives have been found that reduce wash off, thus extending the effective residual life of the applied chemical.

The problem then is to devise formulations of pesticides to overcome so far as possible these limiting factors. This may be accomplished by using the proper ingredients in the original formulation or with the use of additives at the time the spray is mixed. We are now beginning to have a sufficiently good understanding of the chemistry and dynamics of pesticides, so that formulations tailored to the particular conditions of application and environment can be prepared.

Recent Developments in Pesticide Formulations

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 continuous 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 viscous emulsion 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 utilizes a foam containing the chemical, rather than discrete spray particles. Complex glycols and stabilizing agents are used to produce such materials in mechanical sprayers.

An exciting development in pesticide formulation is that of microencapsulation. 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 the 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 incorporated into 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, prevent wash off, and slowing down biological degradation. It should soon be possible, for example, to obtain granular formulations of systemic chemicals that will provide a sustained release that would extend the effective control period by two or three times.

Proper formulation of a chemical as can be seen, requires a number of different additives and agents, each with its own special function. A partial listing of some typical agents used with present day pesticides is given in Table IV together with the function they perform in the formulation. This table is only for purposes of illustrating the type of agents used, the function or role they play in the formulation, and gives only a few examples of the various additives that are available for this purpose. The development of the appropriate formulation for a given set of conditions requires study and experience, together with the knowledge of the limiting factors to be overcome.

Table IV

Some Formulation Additives and Their Function

Agent	Example	Function
Solvent	Petroleum Xylene Ketones	Dissolve and dilute active agents
Surfactants	Soaps Sulfonates Aryl polyoxy ethylene Alcohols (Anionic, cationic, nonionic)	Emulsifiers Wetting agents
Thickeners	Methyl cellulose Gums Water dispersible plastics	Increase viscosity & drop size Reduce drift
Clays	Attaclay Bentonite	Diluents and base for dusts Wettable powders and granulars
Stickers	Glyptal resins Plastics Terpene polymers	Enhance retention

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.

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STORAGE, HANDLING, AND DISPOSAL OF CHEMICALS

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Human and Environmental Exposure

In the distribution and use of pesticides, large quantities of technical concentrate or formulated material must be stored and handled. The material may be packaged in large containers or handled in bulk, that is in tanks or bins if it is a dry powder. In storage, handling, and distribution of these chemicals, there is an inevitable escape of some of the material or there may be accidents or spills.

Sometimes, because of contamination or deterioration it becomes necessary to dispose of bulk quantities of the chemical. Unless the proper precautions are taken, the storage, handling, and disposal of large quantities of chemicals can result in a serious threat to human health and the environment. In this presentation we will review some of those precautions so as to reduce the risk attendant in handling and disposing of bulk quantities of chemicals.

There is always a likelihood of human exposure in handling of chemicals, whether it be transferring it from one container to another, repackaging, or mixing for application. Where technical products or highly concentrated formulations are being handled, the risk of poisoning from exposure is high. Consequently, all precautions of protective clothing, ventilation, and the utilization of mechanical transfer so far as possible is essential. But exposure of humans can come also from spills or disposal of the chemical. Thus, one must be concerned in handling and disposing of bulk quantities of chemicals with environmental contamination such as that of a stream, or food through which other humans may become exposed. It is not only the problem of direct human poisoning, there is also the serious matter of environmental effects from large quantities of chemicals which may range from injury to a few of the more susceptible species, to creation of a virtual biological desert within the contaminated area.

Toxicity and Hazard

Before attempting to discuss specific problems of storage, handling, and disposal of large quantities of chemicals, let us take a moment to review a few basic principles that can serve well in devising safer practices. Everyone knows, of course, that pesticides are classed as poisons. However, we recognize that some appear to be less hazardous than others.

Also experience has shown that some of these chemicals will persist longer in the environment than others. What must be borne in mind, however, is that any chemical in sufficient concentration may be toxic. This is a cardinal principle, and applies whether we are dealing with an individual organism, a population of organisms, or the entire biosphere. Admittedly, it appears obvious that overdosing with a particularly toxic chemical will be injurious but sometimes in categorizing some chemicals as being less toxic than others, we tend to forget that an excessive dose of even so-called safe chemicals can be injurious to the individual or the environment. Further, it must be noted that toxicity can result whether the exposure occurs through the skin, respiratory tract, or by oral ingestion.

A second consideration is that if exposure to a given dose of a chemical produces a perceptible effect, even pleasant, this is a fair warning of potential danger. Continued exposure or higher dose levels may cause much more serious consequences. There are two basic facts pointed up in this instance, one is that there exists a dose-response relationship such that with increasing dose there is an increasing effect. Extrapolating this backward, one can safely conclude that there is also a level of exposure or dose below which there will be no serious consequence. A second fact to be deduced is that at doses sufficient to produce a perceptible effect, there exists the potential of producing an irreversible lesion upon continued exposure. There is, however, an intrinsic protection against toxic action if the dose is low enough. In both living organisms and the environment we find the capability of metabolism, sequestration, and elimination of the offending chemical.

Everyone recognizes that there is a difference among chemicals as regards their toxicity, and a difference among organisms as to susceptibility to a given chemical. This immediately suggests that there is a distinction between toxicity and hazard. Toxicity, of course, is the inherent ability of a compound to produce ill effect at a given dose, whereas hazard represents the probability that a chemical will produce an ill effect. The hazard presented by a given chemical is made up of four distinct features, namely:

1. Intrinsic toxicity.
2. Susceptibility of the species affected.
3. Persistence of the chemical.
4. The mobility of the chemical in the environment.

Thus, we see that the hazard in the handling, distribution, and/or disposal of a chemical involves not only the intrinsic toxicity of the substance, but also the properties of the compound that may lead to its dispersal. For example, in a closed space a highly volatile chemical even if not dangerously toxic, can present a hazard, whereas an even more toxic substance of an extremely low vapor pressure would be minimally hazardous. It is very important to remember that it is the manner of storage, handling, and use that determines whether a chemical is dangerous. With proper precautions even the most toxic and hazardous of chemicals may be handled and used safely. On the other hand, with careless handling and improper precautions even a chemical of low toxicity and hazard can cause serious effects.

Classes of Chemicals and Their Properties

With this as a background, let us then look at the nature of some of the pesticidal chemicals, their properties and the problems these afford in storage, distribution, and disposal. The first chemical class are the organohalogen or organochlorine compounds that have been used for many years as pesticides. Within this chemical class we find a wide range of substances, both in nature and in properties. For example, there are materials such as the chloropropenes and ethylene dibromide used as fumigants through to such materials as DDT, dieldrin and toxaphene. Each represent a different problem in terms of handling and disposal, though it is more likely that storage, handling, and disposal problems would be encountered with the solid organochlorines as represented by DDT, heptachlorotoxaphene and dieldrin.

Next on the list of chemical classes are the organophosphates. This class of pesticide is rapidly supplanting the organochlorine as insecticides for most purposes. The organophosphates are characterized as being more volatile, less persistent, and usually much more toxic than the organochlorine pesticides. These characteristics result in particular problems in handling and disposal. Fortunately, the organophosphates are rather readily hydrolyzed by alkaline media to less toxic products.

Carbamates are other chemical structures commonly found among the pesticides. The N-methylcarbamates are used extensively as insecticides whereas the N-aryl products are more commonly found as herbicides. The dithiocarbamates on the other hand, are almost exclusively effective as fungicides.

There are a number of different chemical classes represented by pesticides. There are amides and analids, triazines, ureas, phenols, substituted analines and heterocyclic compounds. Each of these classes and each compound in the class has a unique set of physical, chemical, and biological properties that must be considered in its storage, handling, and disposal. Fortunately, these properties are rather readily determined making it possible for us to devise the appropriate measures for safe handling and use.

Considerations on Storage of Chemicals

As indicated in the commerce of pesticides, rather large quantities of either technical products or concentrated formulations must be stored in order to supply the distribution channels. Frequently, serious problems arise from improper storage of these chemicals since inevitably some of the chemical will be lost in the handling or spilled through an accident. Wastes from storage and formulation plants also must be disposed of, and this all too often through the public sewer or into public waterways.

Facilities

The location of any storage facility for bulk quantities of pesticides should be carefully chosen, so as to remove it as far as possible

from other human activities, insure that there is proper disposal facilities, and prevent inadvertent public incursion. The site should be well removed from streams or bodies of water, and selected so that the slope or drainage is away from such water bodies. It is desirable also that such sites be of sufficient size to accommodate special treatment areas for disposal of waste and spillage.

The building or facility in which the chemicals are to be stored should be specially constructed for the purpose. If there are a variety of chemicals to be stored in the same facility, the building should be large enough to permit isolation or separation of the different chemicals. Where herbicides and insecticides are to be stored on the same site, separate buildings should be provided in order to avoid cross contamination.

Essential to any well constructed storage building, is a concrete floor well above possible flood levels. The floor should have a smooth finish for easy cleaning and to prevent the chemical from soaking into the concrete. Further, the floor should be sloped toward a drain so that spills and splashes of the chemical can be hosed into the drain. The drain itself, of course, should lead to appropriate carbon filters, and treatment equipment so as to prevent contamination of the sewage effluent. Carbon filters and treatment facilities are simple and inexpensive to construct and install. Storage of barrels or other containers of bulk chemical should be on appropriate pallets for protection of the container.

Other features of a well constructed storage facility include good ventilation, fire control equipment, safety showers, and appropriate security to prevent unwanted access to the 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 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. Naturally appropriate protective clothing should be available for the workers that must deal with such spills.

One further point might be mentioned about storage facilities, and that is to have them adequately marked indicating the nature of the material stored in the case of an emergency, such as a fire or an accident. Emergency workers such as firemen are then better able to deal with the problem.

A few words are in order regarding the containers for bulk chemicals and their storage. Safety requires an insistence that the containers be

durable, leak proof, and impervious to moisture. It is not simply enough to require good containers, there should be periodic inspection of barrels, tanks, and bags in storage to check for leaks, damage, or deterioration.

Disposal of Bulk Chemicals

For a variety of reasons it becomes necessary from time to time to dispose of quantities of pesticides and/or containers used for packaging them. It may be that the chemical to be disposed of is a waste from a storage or formulating plant; the chemical may have deteriorated below a quality acceptable for use, or for some other reason the chemical is no longer useful. The question then is, how to dispose of this chemical without danger to humans or serious contamination of the environment. The ultimate name in disposal, of course, is the destruction of the chemical, but during the destruction process we wish to avoid exposure of humans and the serious contamination of air, water, and soil.

There are four ways of disposing of chemicals, they include: use, chemical destruction, incineration, and soil disposal. Though we will talk in more detail about some of these methods later, it may be worthwhile to point out a few important features of each.

1. Chemical Destruction. Chemical destruction of a pesticide depends upon utilizing specific chemical reactions to destroy the chemical. This may be an oxidation with something like permanganate or chlorate, or it could be as simple a reaction as an alkaline hydrolysis. Chemical destruction, though effective, also tends to be costly in its requirement for equipment, additional chemical, and the final problem of the disposal of the waste following the reaction.

2. Use. Using the chemical as a pesticide is perhaps the most effective and economical means of disposal where such a practice is possible. At the low doses normally used for pest control, the environment through photochemical and microbiological degradation will destroy the material. In the meantime, one has benefited by the pest control from the chemical. The usual precautions in use of chemicals could be observed in disposal in this fashion.

3. Incineration. In this instance the terms incineration or burning do not refer to destruction by open fires or burning such as are seen in a sanitary landfill. When we speak of incineration of chemicals, we are thinking of using specially constructed burners (furnaces) that have a flame temperature of over 800°C, adequate air intake, and a long residence time in the combustion chamber to insure destruction of the chemical. Moreover, such incinerators require suitable smoke stacks with treatment devices to avoid air pollution.

4. Soil Disposal. Properly managed soil disposal is becoming a popular means of getting rid of certain types of chemicals. It is much more effective in disposing of organic chemicals such as many of our

pesticides than it is for disposal of inorganic chemicals such as heavy metals. Soil disposal relies on a combination of chemical treatment and microbiological attack to degrade the chemical to innocuous products. The sites for soil disposal of chemicals must be carefully chosen so as to avoid problems of water contamination; also they should be removed from other sites of human activity and should be large enough to handle the amount of chemical to be disposed of. The site may be set aside indefinitely for chemical disposal, or if properly managed and not over treated, it may be brought back into use for other purposes after a few years.

Disposal of Containers

Examining now some specific cases of disposal problems, consider first the problem of disposing of pesticide containers. Paper and plastic bags used for pesticides should never be carelessly discarded or thrown into ditches, streams, or waterways, but should be disposed of by burial. The burial may be in a sanitary landfill using appropriate additive chemicals to accelerate the breakdown. The bags may also be incinerated if the proper type of furnace is available.

The problem of disposing of glass and plastic jugs, or metal containers, poses a somewhat different problem. Very often the jugs, gallon cans, or drums appear to be attractive for other uses. There have been a number of instances of human poisoning where pesticide containers were put to other uses after they have been emptied of the original pesticide contents. Environmental contamination can result if the containers are carelessly discarded. It is impossible to drain any one of these containers completely empty of the pesticide. Repeated rinsings will help to reduce the amount of pesticide remaining in one of these containers, but even that does not get rid of all of the material. To make disposal of pesticide containers safer, we have come to recommend that each container be rinsed at least three times and the rinsings emptied into the spray tank. The rinsing may be either with water or with oil, whichever is the most effective solvent for the pesticide formulation. If people insist on using these containers for other purposes, a much more elaborate precautionary clean up should be followed. In the case of the organophosphates or carbamates, it should include soaking of the containers in a relatively strong alkaline solution followed by a thorough washing with water and detergent, followed by yet another soaking in which carbon or charcoal is introduced into the water in order to remove the last traces of chemical.

Perhaps the best means of disposal of the larger containers, drums, barrels, and tanks, is to reuse them for the same pesticide. The drums may be reconditioned in a relatively inexpensive facility and returned to use. The reconditioning usually involves steam cleaning, occasionally chaining to remove the plastic liner, followed by relining the drum.

Wastes and Spills

Another problem of disposal is that of waste from storage and formulation plants. If the plant is properly constructed the spills and leaks will be contained on the concrete floor where they may be adsorbed with carbon or a clay, neutralized with lime and this waste

then disposed of by soil degradation at an appropriate landfill 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 to 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.

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 earth floors absorb 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.

Soil Disposal

There are two quite different practices in disposal of chemicals in soil. The one practice utilizes the so called "sanitary landfill" where a pit is dug in the soil and the chemical disposes in the pit. Usually some chemical additive, such as lime and charcoal, are used to accelerate the breakdown of the chemical in this sanitary landfill. The practice then is to line the pit with quantities of lime and charcoal. A layer of the chemical to be disposed of is next placed in the pit, covered with more lime, and a layer of soil used to cover. A second layer of lime is added, then more chemical, more lime, and finally another layer of soil. The site for the sanitary landfill handled in this manner must be chosen with extreme care, since the breakdown of the chemical will not be very rapid, so that some leaching from the landfill may occur causing contamination of ground water and/or nearby streams.

It is recommended that where pesticides or toxic chemicals are to be disposed of in this manner, the individual pit be limited in size and relatively small quantities of chemical disposed of in each pit. The pits should be 10-30 meters apart, have a maximum depth of not more than 2 1/2 meters, and have a covering of 1/2 to 1 meter of soil. The purpose of the lime used in sanitary landfills is to provide an alkaline media that will hydrolyze the organophosphates and carbamates to relatively less toxic products. Moreover, the lime as it diffuses into the soil, encourages microbiological activity that brings about further destruction of the hydrolyzed products. In the case of the chlorinated hydrocarbons, the alkaline media dechlorinates the substance to another product. In some instances, further breakdown occurs fairly rapidly. If rapid breakdown of the chlorinated hydrocarbons is desired, the addition of animal manure or good organic compost plus some fertilizer creates an aerobic condition that brings about fairly rapid degradation of the organochlorines.

The other method of soil disposal consists of distributing the material over a larger area, incorporating it into the soil to a depth of 5 or 6 inches, and, depending on the microorganisms of the soil, breaking the chemical down. Management of such an area by means of adding fertilizer and maintaining soil moisture accelerates the rate of breakdown.

Where organophosphates are to be disposed of in this fashion, the addition of lime at the rate of 2 1/2 tons per hectar will accelerate breakdown. The amounts of chemical that may be applied in using the soil for biodegradation can range from 10-20 times the normal rate of application.

The site selected for biodegradation as described above is very important. Again, it must be removed from other human activities, it should not drain into streams or bodies of water, and some provisions should be made to drain any surface runoff into a sump area before being released. With proper site selection and management, the soil biodegradation technique can be an effective way of disposing of unwanted organic chemicals.

Summary

In the storage, handling, and disposal of chemicals, there are attendant risks for human exposure and environmental contamination unless appropriate precautions are taken. Based on our knowledge of the chemistry of a compound and its toxicology we are able to take those necessary precautions to prevent these risks. The precautions enable us to safely handle and dispose of most chemicals. The steps to be taken include provision of suitable storage space equipped with adequate ventilation, concrete floors, and having appropriate capability for dealing with accidents and spills. Disposal of chemicals involves capitalizing on known chemical and physical properties to bring about degradation. A variety of degradative procedures are known, among them chemical, biodegradation, incineration, and sanitary landfills. Selection of the method of disposal of excess chemical is based on criteria of human safety and environmental protection. Containers afford a special type of problem but correct procedures can be devised for these as well.

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