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Pesticides

by Ladislav Rosival, MD¹

ROSIVAL L. Pesticides. *Scand J Work Environ Health* 11 (1985) 189–197. The last 30 years have been marked by concern regarding the effects of pesticides on human health and on the environment. Unwanted and adverse effects on man and other nontarget organisms have been reported from many countries. The health effects recorded for thousands of people yearly are mainly caused by the inappropriate handling of pesticides or by accidents. The important task is to identify and evaluate the specific hazards of the handling and application of pesticides and the need to collaborate with the World Health Organization (WHO) and other organizations on promoting the health protection of exposed workers. The selectivity of chemical control methods can often be markedly improved by the proper choice of formulation and application techniques and, of course, by an appropriate choice and use of the pesticide itself. This work is an integral part of the international program on chemical safety based on and incorporating current WHO activities. The situation in the developing countries creates a new dimension for the work to be done. In these countries the working populations are affected by the general diseases prevailing in the community, as well as by many uncontrolled hazardous agents at work.

Key terms: pesticide exposure, residues in food, resistance to pesticides, toxicology of pesticides.

One very real problem of today is to guarantee the nutrition of mankind. This guarantee can be achieved through several measures, and one of the most important tools is pesticides. About 80 % of the pesticides used in agriculture today are applied in the developed countries.

Pesticide development has also greatly benefited mankind by improving health conditions through the control of vector-borne diseases, which prevail mainly in tropical and subtropical areas. The number of people threatened or infected by the four main tropical diseases of this type totals more than 1.6 billion, ie, more than one-third of the world population.

But the use of pesticides also involves hazards. Pesticides affect the health of thousands of people throughout the world each year. These effects are mainly caused by their inappropriate handling or by accidents (5). Factors involved include lack of in-service training, insufficient dissemination of information on the properties of pesticides (eg, improper labeling), and technical shortcomings (eg, leaky equipment). Especially hazardous are the application of concentrated formulations with handheld ultralow-volume equipment and the misuse of pesticide-treated grain for consumption.

It has been stated that, worldwide, half a million cases of pesticide poisoning occur annually and one-tenth of them are fatal. Thus far it has not been possible to confirm or substantiate this fact, and it would be very useful to obtain hard data on both the number of people occupationally exposed and the real — not alleged — casualties that occur.

New scientific knowledge has, however, become available during recent years, particularly in respect to (i) the health effects of pesticides in various environmental media, (ii) their pathways from the environment to man, (iii) methods of detecting their hazards in the environment, and (iv) the priorities of research on pesticides. Although only 10 % of the pesticides produced is used in public health, research activity on pesticide safety has tended to be more concentrated to this area than in that of agriculture.

Extensive biomedical research on the effects of pesticides in man from an ecochemical, toxicologic, and epidemiologic viewpoint is a recent phenomenon. The experimental designs and methodological approaches currently in use reflect a sophistication that has offered promising leads for exploration and has provided results of significant importance.

Pesticides are closely related to the increasing use of chemicals in general, and long-term strategies are also needed in this field. Exposure of human beings to pesticides may be occupational (through the manufacture and application of pesticides) or non-occupational (eg, residues of pesticides in food). The environmental aspects of the use of pesticides create special problems.

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Safety in the manufacture and use of pesticides

Manufacture of pesticides

Occupational health programs aim to promote and maintain the highest possible level of health among occupationally exposed workers. Out of this experience in the manufacture of pesticides have come important data concerning the relationship between the nature, magnitude, and duration of contacts with causative agents and work situations and the resulting type and degree of response in man. The systematic collection of measurements of actual exposure to the various hazardous agents and the recording of medical observations on exposed workers have made it possible to demonstrate correlations between the level of exposure and the degree of health impairment (6).

Based on the general conclusions of the Expert Committee on Methods Used in Establishing Permissible Levels in Occupational Exposure to Harmful Agents (7), a project for recommendations of health-based permissible levels for chemical substances has been launched. In the group of pesticides malathion, carbaryl, dichlorodiphenyltrichloroethane (DDT), aldrin, and dieldrin were chosen, and a corresponding document for health-based permissible levels has been prepared.

With regard to safety in the manufacture of pesticides, it can be stated that there should not be any special health risks in modern pesticide factories if safety regulations are observed. But it must also be remembered that exposure during this work may not only involve the final pesticide products, but may also include an intermediate or intermediates, often highly reactive, used in their synthesis.

Occupational application of pesticides

Occupational exposure to a "cocktail" of pesticides can occur in any of many phases. It starts with the manufacturing process, continues with transport to the storage or application site, and finishes with the transfer from containers to the application equipment. The next phases are application, field work involving contact with residues, drift of the pesticide out of the application area, disposal of the unused chemicals or containers, clearing and repair of application equipment.

The greatest hazard is usually not the application itself, although some such procedures incur special dangers, for instance, the serial application of pesticides, which creates problems not only occupationally but also ecologically. (More than 90 % of the used pesticides do not reach their target). Instead the greatest hazard exists during the handling and mixing of concentrated formulations and the filling of mixing tanks and spray equipment. A careful selection of the compound is essential in order to mini-

mize the exposure and the potential hazards. Additional critical points are environmental aspects (especially meteorological conditions), the position of the worker, the physical effort involved in the work, worktime duration, personal protective measures, and the attitude of the worker.

The physical form of technical grades of pesticides varies from volatile liquids to semiliquids to crystalline solids. The components of pesticide formulations consist of the pesticide, the "carrier" (organic solvent for an emulsifiable concentrate, mineral clays for wettable powder, etc), surface-active agents and other ingredients, stabilizers, dyes, etc. New developments in formulation technology should lead to further improvements in the safe handling of pesticides.

The risk of illness attributed to pesticides varies with the situation (field workers' exposure to residues on a crop, exposure of a pilot of an agricultural aircraft, etc). Specific problems requiring special toxicologic surveillance are involved in the use of pesticides with a lower acute toxicity in public health activities. During such activities the general public is in more intimate contact with the pesticides, for example, when homes are sprayed and the very old, very young, and sick are exposed. Furthermore, users may be exposed for a long time, sometimes exceeding 15 years, if some types of vector-control pesticides are deliberately added to water, which might be drunk.

Prevention of pesticide hazards

The safe use of pesticides depends on the availability of up-to-date information on the pesticides involved, the choice of pesticide, storage conditions, and the conditions at the sites of use.

The key to safety is control of the level of exposure to a given pesticide. This level is usually subject to wide variations, depending on some or all of the following conditions: (i) the type of formulation; (ii) the method and rate of application and the equipment used; (iii) environmental conditions, such as prevailing winds, temperature, and humidity; (iv) the physical posture and individual constraints caused by variables such as the height of a crop or the type of house to be sprayed; (v) the duration of work; (vi) the use of personal protective devices, eg, gloves, other protective clothing or face masks; and (vii) the attitude of the operators (8).

The education and training of pesticide sprayers, supervisors, and even the general public about the use of pesticides forms the first line of defense against pesticide hazards (2). The content of educational programs on the safe handling of pesticides should be based on the principles of general hygiene, an assessment of hazard based on toxicity (including the classification of toxicity), and on exposure in a given situation.

The necessary toxicity data can be provided by the

manufacturing or marketing company, by regulatory authorities, or by international organizations. Data on exposure and dose-related effects, however, should be generated locally whenever worthwhile. Cooperation between industry, international organizations, and local institutions is essential. Local experts should finally evaluate the health hazards in light of local conditions.

Before an educational program to improve the handling of pesticides is started, the level of existing knowledge and the attitude of the people concerned should be evaluated. Such an evaluation is an indispensable guide for the design and implementation of an educational program.

Educational programs should be constructed nationally, or even locally if it is possible to take cultural factors into account. Flexible programs, such as the multilevel modular course of the World Health Organization (WHO), can provide an outline for instruction. These courses have to be translated and transformed into national terms and adapted to national conditions however. For the time being, it may not be possible to educate all pesticide handlers adequately in certain areas. If this is the case, efforts should at least be made to educate the responsible field supervisory staff. For the handling of highly toxic formulations, a system of training leading to the recognition of application personnel and vendors should be adopted whenever possible.

The manufacturers and suppliers of pesticides should be encouraged to contribute as much as possible to safe handling. Several aspects need to be considered, especially the type of formulation, packaging, and cooperation between the manufacturers and suppliers of pesticides and the manufacturers and suppliers of application equipment. Companies should not commercialize formulations that are known to be unsafe under certain conditions.

Education on the hazards of pesticides requires a very comprehensive approach based on the following three main objectives: to inform, to motivate, and to set into action. As to the first objective, we must be aware of the fact that dangers of pesticides to health are often caused by imperfections in our own behavior, often linked with ignorance and carelessness that parallel inadequate precautions of national and other authorities. In this connection we must not separate protection from the promotion of health, and we must see it as a holistic effort which combines actions concerning health, education, economics, etc.

The second objective, motivation, involves creating a desire among people to comply with the standards for a rational use of pesticides as an integral part of rules for a healthy life. Educational programs are needed to reinforce the process of development. Radical changes may be needed in methods of instruction to make them more relevant to socioeconomic development and to new technologies. Mo-

tivation may be achieved effectively from good examples and from peer acceptance which illustrates that education is really an everyday practical matter rather than a course of lectures.

The third objective is to set into motion. The problem is not only that of educating the public, but also of changing the undergraduate and postgraduate teaching in medical and other schools. The prevention of pesticide exposure and hazards has been neglected in many countries, sometimes with tragic consequences for the population.

Finally, we know that no human activity can be completely free from risks, also in the case of pesticides. Although risks cannot be totally eradicated, they can be identified, measured, investigated, evaluated, controlled, and reduced. In the evaluation of risks the subjective assessment of risk is important, especially in terms of whether the risks taken are voluntary, whether the hazards are familiar, whether individuals or the community is at risk, the cause of the hazard and the size of the problems. It has been shown that some psychological aspects are related very closely to hygienic education. Each educational message interacts with a social context also in the case of pesticides.

Monitoring of exposure

The best method of detecting long-term effects of pesticide exposure still involves a good medical history and clinical examination of exposed persons. The laboratory procedures which should be used are difficult to agree upon; they should include blood chemistry, assessment of liver function, and pesticide blood levels if possible. It is important to determine any decrement in the physical and mental fitness of the exposed workers and their work capacity. In the final analysis, the ultimate assessment relies on biological studies in which provision has been made for a comparison of exposed persons with suitable referents (controls).

For each individual it is desirable to establish pesticide levels of exposure and the body content permissible for a lifetime, as well as the permissible levels for short- and long-term occupational exposure. For this purpose one must establish the dose-response relationships, ie, the relationships between parameters of exposure (body content, residue levels in tissues) and parameters or response (effects) for each individual compound.

Parameters of effects differ for various groups of pesticides (organochlorines, organophosphates, etc). The most sensitive indicators of effect may not be the most relevant parameters because (i) they may — in the light of current knowledge — not appear to be related to vital effects on health and (ii) they may be impractical for routine medical supervision or for public health monitoring. In such cases the study should be directed towards finding the relevant parameters.

The mere presence of pesticides in human tissue does not in itself indicate an effect; it only indicates exposure and subsequent absorption. Only when the concentration(s) in the target tissue(s) exceed(s) a certain level, specific for each pesticide and for each target tissue, does it (do they) begin to be associated with effects. At equilibrium these levels will probably be related to other levels of exposure.

In adult workers the highest dieldrin concentration in whole blood consistent with an absence of any effects has thus far been established to be at least 0.105 $\mu\text{g}/\text{ml}$. This finding pertains to parameters of health (incidence of disease, sickness absenteeism), biochemical profile, and some tests of enzyme induction.

For DDT the same level is estimated at between 0.2 and 1.0 $\mu\text{g}/\text{ml}$. A better estimate should however be made in a study on volunteers rather than on exposed workers. A study of exposed workers can only provide an enzyme induction "threshold level" for DDT, but not for dichlorodiphenyldichloroethylene (DDE) or a relevant mixture of DDT and its metabolites as they occur in food. Such a study would suffice to furnish the data on which the protection of exposed workers can be based. As regards the general population, only a supervised study on volunteers administered a relevant mixture of DDT and its metabolites as occurring "naturally" in the daily diet may provide an answer to the question. The "threshold level" derived from this study should then be related to the blood levels at equilibrium. As regards chlordane, endosulfan, endrin, heptachlor, methoxychlor, and the various isomers of benzene hexachloride (BHC), the data available are inadequate to allow any conclusions to be drawn.

The relationship between exposure, cholinesterase-activity depression, and changes in the electromyogram should be quantitatively established, both as regards levels and duration of exposure and the relation between the onset of changes and the time to reversal. Finally the significance of the various modes of changes in the electromyogram should be clarified after comparison to changes — if any — occurring under physiological conditions, and exposure to other compounds such as ethanol. The effects recorded in the electromyogram should be followed up by other electrophysiological studies, eg, electroencephalography, electrocardiography, and electroretinography. In addition studies of tendon reflexes and metabolites should be carried out.

It is also desirable to examine chronic effects — if any — on renal and cerebral function from long-term exposure to some organophosphate insecticides and carbamates. A diagnosis of insecticide poisoning should be based on clinical signs and symptoms consistent with intoxication following overexposure to the insecticide. This diagnosis has to be confirmed by biochemical and analytical evidence of excessive absorption of the insecticide.

In the case of organochlorine insecticides the blood levels can be determined, and for some of them threshold levels (below which a diagnosis of intoxication is unlikely) are known, at least for single compound exposure.

As for organophosphates a diagnosis of intoxication is definitely untenable if at the time of signs and symptoms the cholinesterase activity in the blood is not considerably inhibited. The same probably applies to carbamates.

A long-term study of occupationally exposed subjects should have a duration of at least 9–10 years (one-eighth of a lifetime) at a level of exposure of at least 20 times the exposure of the general population and, if possible, should use specific parameters indicated by animal experimentation. As regards the occurrence of liver microsomal enzyme induction, however, the period of the study may be relatively short and may be a matter of weeks.

A listing of subjective complaints in answer to leading questions is an unreliable method of study, even when a reference group is used. Only when extensive questionnaires (constructed so that a particular answer can be double-checked) are filled out can misleading answers caused by occupation and the situation of the worker, as well as of the preconceived ideas of the examiner, be, perhaps, avoided. Comparison of disease patterns based on sickness absenteeism will also lead to invalid conclusions if no allowance is made for the major factors influencing this parameter, such as selection, the socioeconomic situation of the worker, and the social insurance system. In addition conclusions regarding hazards to the general public from pesticide exposure are invalid if they are based on unquantified observations of exposed workers. The incidence of subjective symptoms or objective signs in exposed subjects does not allow any conclusion as long as no comparison has been made with a valid reference group.

Positive epidemiologic observations on workers with multiple exposures indicate that further work is needed on the individual compounds, and they do not allow any conclusions about any individual agent nor a generalized conclusion on the whole group of compounds.

Negative observations, if based upon a well-conducted epidemiologic study, are highly important. Such studies should also be published, as they may narrow the range of existing uncertainty. However, in extrapolating these data to the public, we should always bear in mind that, although the general population may undergo similar multiple exposure of a lower degree, the quantitative relationships within this mixed exposure may differ.

The relevance of epidemiologic toxicology in occupational exposure for the area of public health is highly relevant because (i) the effects of longer-term occupational exposure become evident much earlier during the development and industrial life of the

compound than they do from public exposure, (ii) at the higher levels of occupational exposure subclinical effects may be detected by a special study which is not possible among the general population, where too many variables play a role, (iii) indispensable and valid reference groups can more easily be found for industrial circumstances, (iv) measurements of exposure are often more accurate in occupational exposure than in public communities, and (v) with the use of an appropriate conversion factor effect and no-effect exposure levels can be extrapolated from industry to the community (9).

There are no known studies indicating effects on the health (physical, mental, and social well-being) of subjects with prolonged exposure to cholinesterase-inhibiting compounds as long as the plasma cholinesterase inhibition has never exceeded 30 % of the individual preexposure level. Effects in electromyograms have been reported within this range, but their health significance must still be determined.

Evidence has been presented in various studies that, in workers with prolonged multiple exposure to pesticides, deviations may occur in the biochemical blood profile (protein, lipids, enzymes) in comparison with levels in matched reference groups; the same applies to evidence of enzyme induction. There is insufficient knowledge regarding dose-response relationships and whether the mixed exposure or the individual pesticides are the causal factor. The average levels in workers do not usually exceed the range occurring in unexposed workers; the clinical significance of the deviations is not yet clear however. Epidemiologic studies, particularly longitudinal periodic examinations, should be promoted among exposed workers and valid referents.

Some authors have shown that deviations may occur in the biochemical profile (enzyme levels, lipid metabolism) in workers exposed for many years to mainly one organochlorine pesticide and closely related compounds in comparatively high doses. The dose-response relationship and the clinical significance have not yet been adequately established, and further epidemiologic research is needed.

Observations of workers exposed to pesticides do not indicate that similar deviations are likely in the unexposed general population; there is a need for epidemiologic studies of dose-response relationships in groups of subjects over the whole range of "normal" exposure, slight exposure, and higher exposure. A model scheme has been recommended by a workshop organized by the Scientific Committee on Pesticides with regard to the epidemiologic toxicology of pesticides (9).

Other aspects of the safe use of pesticides

Field surveys of pesticide exposure. In the last few years surveys have been organized to study exposure under actual field conditions in both agriculture and among the general public.

The methods recommended for the toxicologic surveillance of exposure of organophosphorus pesticides have been set out in a standard protocol by WHO (19). The protocol was developed in collaboration with the Scientific Committee on Pesticides. This approach will be adapted for pesticides belonging to other chemical groups in the future if a means of measuring absorption in man becomes available. This evaluation scheme is largely responsible for the safe and efficient use of pesticides in public health programs throughout the world.

Field studies are essential to gather information on exposure patterns of pesticides, their possible biomedical effects, and the development of methods for the occupational surveillance of field workers. These studies would enable the hazard to be assessed and the routine surveillance needed for occupational groups to be defined. Field studies should be carried out under representative conditions in which both human and environmental factors are included. Their design and the protocol should take into account (i) specific properties of the pesticide; (ii) symptomatology and the mechanism of action, if known, of the pesticide, as derived from experimental toxicology; (iii) method of application; (iv) local and ambient conditions; and (v) the cultural characteristics of the workers. Such designs should be as flexible as possible to anticipate unexpected events, but they should always meet the scientific objectives set.

Field studies should be undertaken wherever possible with the approval of governmental authorities and, if possible, also in consultation with international organizations, such as WHO, the International Labour Organisation (ILO), the Food and Agriculture Organization (FAO), etc. The importance of good public relations is stressed (4).

Treatment of insecticide poisoning. The treatment of poisoning due to organophosphates, carbamate, and organochlorine insecticides has been summarized in Annex 2 of the third report of the WHO expert committee on vector biology and control (8).

Expertise in toxicology. Experimental animal toxicology should be carried out in experienced and recognized laboratories. The results should then be valid everywhere, irrespective of where they were obtained. An increasing number of accidental releases of chemicals, including pesticides, into the environment has resulted in adverse effects on health of epidemic proportions. It is therefore very important that international cooperation be able to provide rapid and effective responses in emergencies and the development of arrangements for mutual assistance between different countries (4).

Evaluation of toxicity and hazard. There are many classifications of the toxicity and hazards of pesticides. The WHO classification is the most relevant guideline for use in occupational exposure, and it has already been adopted by a number of countries. More data derived from long-term toxicologic studies and actual exposure in laboratories, plants, and the field should be considered as they become available.

During recent years, the attention of toxicologists and chemists has been drawn to impurities in technical pesticide preparations. In the toxicologic classification of pesticides this problem assumes enormous importance. There are two main sources of impurities in technical pesticide products. First, the raw materials for pesticide production may contain impurities. For example, the amines used in manufacturing alkyl amine salts of phenoxyalkane carboxylic acids may contain corresponding N-nitroso alkylamines, or the production of camphechlor (toxaphene) by chlorinating camphene of technical quality only may lead to impurities. Second, the manufacturing technology may include chemical reactions which inevitably result in reaction products containing by-products. Some examples are the formation of S-alkyl isomers in organophosphorus thioates and dithioates, ethylthiourea formation in ethylene-bis-dithio-carbamates (EBDTC) production, the formation of N-nitrosoalkylamines during the production of dinitroaniline herbicides (trifluralin, benfluralin, isopropalin), and the formation of polychlorinated dioxines and polychlorinated furans during the production of pentachlorophenol, hexachlorophene, and 2, 4, 5-trichlorophenoxyacetic acid. Secondary sources of impurities include (i) the unsuitable formulation of the technical-grade active ingredient (eg, the isomerization of organophosphorus thioates and dithioates and the formation of hydrophilic degradation products leading to an alternation of toxicologic and pesticidal properties), (ii) unsuitable tank-mix preparation before practical application (eg, ethylthiourea formation from EBDTC fungicides), and (iii) unsuitable storage of formulations (eg, chemico-physical transformation of an active ingredient).

Evaluating the biological activities of interfering substances present in pesticide preparations is of great importance from the toxicologic point of view. It represents a new attitude contributing to the elucidation of the mechanism of action of such substances and enabling the creation of objective criteria for their toxicologic classification (3).

A number of individual studies have been performed that attempt to reveal possible teratogenic, mutagenic, or carcinogenic activities of a series of pesticides. These investigations suffer from the following weaknesses:

- The methods used for the experimental studies are not uniform and therefore the data are not always comparable.

- The experimental studies have not been designed in relation to the purposes of industrial hygiene.
- There are no criteria, or even guidelines for criteria, available for the interpretation of results.
- The data from the research already done in the field of nutritional toxicology (food additives and pesticide residues) should be used, but additional information is necessary before they are applicable in occupational health activities.
- Toxicity testing should be redesigned with better consideration of how the hazards operate. Prediction of a hazard cannot be based solely upon oral toxicity tests. Dermal and inhalation toxicity of formulated products in concentrations relevant for actual situations should be established also. Concentrations of the agents in the air in field use and dermal contamination should be also measured.
- Data derived from field studies in one culture (education, habits, training) and climate are not necessarily applicable in another.
- It is not possible to calculate the toxicity of a mixed product from the toxicity of separate technical compounds; however such calculations may yield a first approximation.
- Permissible limits valid for industrial production are often not applicable to field conditions because of differences in the duration of exposure, intermittent exposure, mixed exposure, sequential exposure, and other aforementioned interfering factors.
- Biological exposure tests may prove to be an important tool for the protection of health. Application and development should be encouraged.
- In addition a minimum time for safe reentry to work should be developed and incorporated into legislation.

Mere classification cannot replace the risk-benefit assessment that should accompany the use of any pesticide. The hazard has to be considered in relation to the level of training of the applicators and the expected benefits.

Technical materials used for the determination of toxicologic indices should be clearly characterized. Toxicity data on formulations should be made available as much as possible. Toxicologic values should be measured and not only calculated. In the case of worker exposure cutaneous absorption is the most relevant parameter. There is a greater, but more easily controllable hazard for the manufacturer and formulator than for the applicator.

Methods should be developed for the assessment of worker exposure. At the same time the parameters used to assess worker exposure should be adapted to wide-scale application. More attention should be paid to dose-response relationships in human studies.

Safety of the food consumer

Food consumer safety is one of the most hotly discussed questions in scientific circles, in the media, and among the public today.

The assessment of the consumer hazards arising from very small quantities of pesticides in food and the environment is an important part of the overall risk-benefit evaluation now regarded as essential before a pesticide can be introduced in most countries. The availability of reliable data on the quantities of pesticides occurring in food, feed, and the environment is a basic requirement for a realistic estimate of human exposure. Increasingly, the demands of national registration and health authorities include residue data on treated crops and commodities and in water, soil, air, wildlife, and other components of the environment. These authorities reach conclusions and make decisions only when satisfied that the data are indeed reliable (1).

For many years national authorities and official institutes in several countries have constantly monitored the presence of pesticide residues in food and the amounts of residues which reach consumers. They analyze thousands of samples each year.

Carefully collected data have recently been published by the Residue Committee of the International Group of National Associations of Manufacturers of Agrochemical Products in a brochure entitled "Pesticide Residues in Food." After a review of (i) the data submitted by manufacturers on applications for registration, (ii) the toxicologic aspects of the presence of residues, and (iii) various governmental contributions, a method for deriving acceptable daily intakes (ADI) and maximum residue levels (MRL) is presented. The study reviews the situation in the following countries: Australia, Brazil, France, the Federal Republic of Germany, Guatemala, Hungary, Ireland, India, Japan, Kenya, The Netherlands, New Zealand, Sweden, Switzerland, the United Kingdom, and the United States. The data sources, given at the end of the review, are many, and particular importance is given FAO/WHO documents.

In developed countries the number of cases of excess residues is showing a tendency to decline, mainly because persistent pesticides are no longer used. Instead pesticides effective at very low application rates are gaining more importance.

On the other hand many developing countries do not possess adequate facilities to undertake pre-registration trials on pesticides and their formulations, toxicity tests, or pesticide residue analyses of crops, stored food grains, animal products and processed food products. Neither do they have the capacity to generate appropriate data on the intake of pesticide residues and the impact on the environment. FAO/WHO should intensify their assistance to the establishment of suitable facilities for these activities either at the national or regional level. FAO/WHO

and other international organizations, such as various bodies of the United Nations, should intensify their assistance to training personnel involved in such programs in the developing countries. Especially, the safe application of pesticides, the techniques of sampling, and the methods of analysis and documentation should be taught.

Environmental aspects and pesticide resistance

In the last several years pesticides have caused many unwanted and adverse effects on organisms other than target organisms. These effects include excess mortality and a population decline of fish, birds, crustaceans, and nontarget insects; reduced reproductive success or potential among birds and fish; loss of plant species; and pest resurgence. This is the consequence of applying modern technology in agriculture (large fields, simplified crop rotation, new crop varieties, use of mineral fertilizers, and the broad use of herbicides). Some ecological effects are reversible at present but may become much less so in the not too distant future (5).

Of great concern is the increasing pesticide resistance of vertebrate and invertebrate crops, pests, and disease vectors (of greatest significance in developing countries) and also of some plant species. Currently there are at least 428 resistant species (in 1965 182) from many arthropods, especially insects. Integrated pest management, which is an ecological approach, embracing the appropriate use of pesticides in good agricultural practice, will help to minimize resistance problems, but close cooperation of all concerned with the crop, pest, or vector will be needed.

The international dimension of pesticides

Four interrelated aspects of the use of pesticides have significant international dimensions. First, food is a major commodity of international trade, often consumed in a different national jurisdiction from where it was grown. In this regard pesticides are international in both the necessity to protect the health of the consumer and in the need to facilitate trade in food. Second, the pests themselves are often international and are found in different countries growing the same crops. Third, pesticides spread from the country of discovery to other countries with similar problems. Fourth, concern has grown in recent years as to the potentially harmful effects of pesticides on man and ecosystems. The recognized potential of the harmful side-effects that may result from pesticides in the environment are as follows: (i) abiotic environment (residues in air, water, and soil); (ii) plant changes (residues, phytotoxicity); (iii) physiological changes in animals, morbidity and mortality among animals, insect population changes, etc (residues in

tissues and organs); (iv) morbidity and mortality among humans (residues in the organism, effects of occupational exposure); (v) possible changes in the biological value of food (residues); (vi) development of resistance among target organisms.

The international dimension of pesticides is reflected in the number of international organizations with some direct program concerning these compounds. In the report given by the Director General of WHO, Dr Mahler, to the 27th World Health Assembly, we can read the following statement:

While the approach of the past, i.e. to deal separately with problems of air, water, food and the home and work environment is still valid as regards legislation, and planning and enforcement of programmes of environmental control, it is now recognized that only a comprehensive view of ecology and the effects on man of adverse conditions in the total environment will provide an adequate basis for the assessment and prevention of long-term environmental risks to which man is exposed.

In its decision of May 1981, the Governing Council of the United Nations Environment Programme (UNEP) requested the Executive Director to submit to it a list of environmentally dangerous chemical substances, harmful at the global level, to which environmental policies should pay special attention. Pesticides were included among the six reported groups of chemical substances. Chemicals that are widely distributed in the environment in significant quantities by human activities represent potential threats to ecosystems, as well as to human health. The choice of chemical substances and processes listed in this report reflects the need to protect ecosystems and populations of nonhuman organisms *per se*, as well as human health.

Recommendations of an expert meeting of WHO, convened in Geneva in 1983 with regard to pesticides, are as follows:

1. Sound pest management practices should not rely on pesticides alone as the primary means of pest control. Full use should also be made of biotic factors in the environment and other suitable methods by adopting the principle of integrated pest management. In any case special attention must be paid to the improvement of pesticide formulation and application techniques.
2. The marked variation in the susceptibility of the world's ecosystems to pesticides necessitates a full appraisal of the local ecosystem conditions prior to the use of chemical control methods; international organizations should be prepared to assist governments to make such appraisals.
3. National authorities and international organizations should make increased efforts to train field workers and disseminate adequate information on the occupational and public health implications of pesticide use. The Code of Conduct on Distribution and Use of Pesticides, which is currently

being developed under the auspices of FAO and other international organizations, is particularly relevant in this respect and should be implemented.

There are no safe pesticides, only safe methods of application. Pesticides have been the object of considerable controversy in various countries in the past. It will be the same in the future. It is sometimes said that we have only two options, that is, to die without pesticides as a result of starvation or to die as a consequence of the intoxication of pesticides. I think a third possibility is to live with pesticides in coexistence because we know that the biological form of pest control is still in an embryonic stage of development. The use of pesticides sometimes raises emotions via the media. We, as scientists, have a great responsibility not only to present facts but also to educate the public.

The efforts of the United Nations Environment Programme, the World Health Organization, and the Food and Agriculture Organization of the United Nations in this field are recognized and highly appreciated and should be strengthened.

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