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# **SAFE USE OF PESTICIDES**

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Fourteenth Report of the  
WHO Expert Committee on  
Vector Biology and Control



**World Health Organization**

**Geneva 1991**

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# WHO Expert Committee on Vector Biology and Control

Geneva, 5–13 September 1990

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## 1. **Introduction**

The WHO Expert Committee on Vector Biology and Control met in Geneva from 5 to 13 September 1990 to examine recent developments in the toxicology of pesticides used in vector control, to advise on their safe use, and to consider the various ways in which Member States can ensure that pesticides are used safely.

The meeting was opened by Dr N.P.Napalkov, Assistant Director-General, on behalf of the Director-General. He noted that the WHO Expert Committee on Insecticides had held its first meeting in 1949 to consider the toxic hazards of pesticides for man and other related problems. The Committee had met at frequent intervals until 1976, when it was replaced by the Expert Committee on Vector Biology and Control. In addition to considering the safety aspects of the use of pesticides in public health, meetings of the Committee had considered other aspects, such as evaluation of the risks arising from the use of pesticides in agriculture and other fields, and that trend was continuing. In all these matters, however, a scientific approach to the problem of pesticide safety was essential in order to assess the potential risks involved in the permanent exposure of the public to pesticides in the environment or as contaminants in food.

It must also be borne in mind that Member States frequently had to contend with public pressure to limit the use of pesticides on the one hand, while on the other controlling vector-borne diseases more effectively and increasing production of food and fibre.

## 2. **Trends in pesticide use**

The Expert Committee on Vector Biology and Control has always realized that the achievement of its principal objective – the control of vector-borne diseases – depends to a large extent on the use of pesticides. However, these chemicals must be distributed, stored and used with care to avoid any adverse effects on users, the general public and the environment.

In the six years since the Committee last discussed the safe use of pesticides, few new compounds have been introduced operationally for vector control, possibly because only a small proportion of all pesticides are used in public health and vector-control operations. Industry finds it uneconomic to develop new pesticides for use in public health unless there is also a potential market for their use against agricultural pests.

On the other hand, while residual spraying, space spraying and application of larvicides remain the main methods of pesticide application in public health, a number of alternative methods have been introduced, including the use of impregnated bednets and other materials, and the use of repellents. More important, advances have been made in the biological

control of vectors by means of bacterial larvicides, and in environmental control methods such as the use of expanded polystyrene beads on the surface of water to prevent mosquito breeding. Considerable research is continuing on these alternatives. Different chemical and nonchemical control methods can be used for different aspects of vector control, the combination of methods being referred to as integrated vector control.

The acceptance of integrated control has proved slow and reliance is still mainly placed on chemical methods. Biological control of blackfly larvae by *Bacillus thuringiensis* H-14 in the onchocerciasis control programme has been the outstanding exception. One of the reasons for reluctance to use the alternative methods may be that they are more costly than the use of chemicals.

World prevalence of vector-borne disease is high. After the initial dramatic reductions in incidence during the 1950s and 1960s, and a period of relative stability in the 1970s, the number of cases has tended to rise in recent years. This is probably due partly to the rise in world population, which has led to an increase in the susceptible population, especially in endemic areas, and partly to an increase in disease vector populations. The situation is complicated by a marked trend towards urbanization in many developing countries, for which vector-control programmes have been unprepared.

The world's most widespread health problem is probably malnutrition. It has been estimated by the Food and Agriculture Organization of the United Nations (FAO) that despite the use of pesticides about a quarter of harvested crops are lost to insects, rodents, birds and spoilage. Pesticides are needed to stem these losses, as well as for plant protection.

In recent years, there has been increasing public concern about the safety of chemicals of all types. Pesticides are an important class of chemicals to which everybody is exposed to some extent. Their potential hazards can be scientifically assessed on the basis of the considerable toxicological and human exposure data available. Both locally and nationally an effort should be made to allay public fears by providing reliable scientific information on the need for pesticides and their safe and rational use. The task of the Committee thus remains as pertinent to the world situation today as it was when the topic of safe use of pesticides was first discussed by a WHO Expert Committee over 40 years ago.

### 3. **International activities for promoting pesticide safety**

In response to the public concern in Member States, a number of international and nongovernmental organizations have adapted their programmes to address the issue of safe use of pesticides.

### 3.1 International organizations

#### 3.1.1 *World Health Organization*

Within WHO, the evaluation of hazards to humans and the environment from pesticides, the promotion of the safe use of pesticides in vector control and agriculture, training and education, have been included among the tasks of the International Programme on Chemical Safety (IPCS), which is a collaborative programme of ILO, UNEP and WHO. Technical collaboration with programmes on various vector-control activities will be maintained.

In view of documented evidence of pesticide poisoning in the Eastern Mediterranean Region, the Regional Office and Member States are concentrating on training national technical staff and providing the public with information on the safe use of pesticides. The WHO Multilevel Course on the Safe Use of Pesticides, which is being used as the model for training, needs to be updated and it is recommended that this should be given priority. The Region is also providing technical support for field trials of new formulations of pesticides, with a view to preventing or delaying the evolution of resistance in disease vectors to the safer cost-effective pesticides now being used.

The WHO Regional Office for Europe has recently cosponsored an International Centre for Pesticide Safety in Milan, Italy. The Centre will provide information, research, training and laboratory assistance to countries in the European Region.

#### 3.1.2 *Food and Agriculture Organization of the United Nations*

Since the adoption in 1985 of the International Code of Conduct on the Distribution and Use of Pesticides (*I*), FAO has continued its efforts to strengthen government capabilities in regard to the registration, control and safe use of pesticides and is receiving support from governments, industry and nongovernmental organizations.

A comprehensive set of internationally agreed technical guidelines provides the basis for implementing the provisions of the Code; recent examples include guidelines on personal protection when applying pesticides in hot climates, the prevention of groundwater contamination, model national legislation for the control of pesticides, and other guidelines related to the safe use of pesticides in agriculture.

A prior informed consent (PIC) procedure has been introduced into the Code. One of its main provisions is the notification of all Member States of a decision by any State to ban or severely restrict the use of a pesticide. Notifications will be processed by a joint FAO/UNEP programme, and will be accompanied by information on the reasons for the ban or restriction, complementary information and other relevant material, including mention of alternative substances.

The Committee recognized that the International Code of Conduct offers a practical and effective means of regularizing the introduction and safe use of pesticides by Member States. Certain provisions of the Code call for the toxicological evaluation of pesticides in relation to human exposure or for registration and control purposes. For example, evaluation will be required to test the validity of the reasons put forward for a ban or restriction of use. In such cases, general acceptance of a decision will be greatly facilitated by more active and extensive WHO involvement in the assessment.

### **3.1.3 *United Nations Environment Programme***

The International Register of Potentially Toxic Chemicals, which is part of UNEP, is closely associated with FAO in the PIC procedure, as part of its work on the implementation of the London Guidelines (2) concerning the exchange of information on banned and severely restricted chemicals in international trade. IPCS is expected to play a more significant role in future PIC work by providing information and advice on the effects on man of exposure to these chemicals.

### **3.1.4 *International Labour Organisation***

ILO has recently adopted a Convention and Recommendation concerning safety in the use of chemicals at work, and is preparing a Code of Practice to guide Member States in drafting national legislation and establishing the infrastructure needed to deal with chemical safety. Other guidelines are being drawn up on the use of agrochemicals. It is intended to provide training on management of chemical risks in the workplace and information on practical methods of preventing harmful effects. In consultation with other organizations and within the framework of the IPCS, criteria for the classification of hazardous chemicals, including pesticides, will be prepared.

### **3.2 *Nongovernmental organizations***

The International Group of National Associations of Manufacturers of Agricultural Chemicals (GIFAP), a nongovernmental organization in official relations with WHO, is promoting safety in the use of pesticides by producing brochures and carrying out field studies on the efficacy of protective clothing in tropical conditions. All its members have agreed to comply with the relevant provisions of the FAO International Code of Conduct.

### **3.3 *Coordination of activities***

These international activities are to be commended, but care is needed to avoid overlap or conflict in the advice given by the different organizations. Even though each addresses a different section of the population, continuous collaboration is essential. In this respect, WHO has gained considerable experience over the last 40 years in preventing adverse

effects from the pesticides used in vector control and has recently become more involved in assessing the potential effects of agricultural pesticides on humans.

Assessment of the risk of pesticides for humans is often based mainly on interpretation of data obtained from animal experiments. This will probably continue. Nevertheless, differences in the responses of different species to chemical exposures are difficult and often impossible to quantify, so that great caution must always be exercised when animal data are used as a basis for predicting possible effects in humans. Predictions are markedly more reliable when human data are available, especially when exposure or actual dose can be measured.

#### 4. **The WHO Pesticide Evaluation Scheme (WHOPES)**

In 1960, WHO established a Pesticide Evaluation Programme, which screened over 2000 potential vector-control agents. In 1982, the Programme was reorganized as the WHO Pesticide Evaluation Scheme (WHOPES), with a view to maintaining the interest of the chemical industry in submitting pesticides proposed for public health use and speeding up the evaluation of new compounds with demonstrable pesticidal activity against vectors of human disease and nuisance pests. It was hoped that this would foster collaboration between governments, industry and WHO in conducting field trials of promising vector-control agents and strengthen quality control of pesticides in developing countries, so that ultimately pesticides could be produced that would be safe and effective when transported, stored and used according to instructions.

National teams or institutions where the trials are carried out, industry, WHO Collaborating Centres, associated laboratories and universities, together with WHO staff and consultants, participate in the operation of the Scheme.

WHOPES consists of a four-phase programme of evaluation and testing:

- Phase 1 covers laboratory testing to determine the efficacy of pesticides, cross-resistance to them in target species and their acute toxicity for laboratory animals.
- Phase 2 comprises evaluation of the safety of the formulations for users, and small-scale field-testing of pesticides against natural populations of vectors, nuisance pests and intermediate hosts.
- Phase 3 involves a large-scale trial or a series of medium-scale trials of pesticides, with entomological evaluation, safety assessment and possibly epidemiological studies, conducted jointly under field conditions by WHO and national authorities, with the financial and technical support of industry.
- Phase 4 is concerned with the drawing-up of specifications for active ingredients and formulations for public-health use, including chemical

and physical methods of analysis to support quality control procedures when pesticides are purchased. Specifications are published in a regularly updated manual (3).

Since the inception of WHOPEs, 65 new compounds have been submitted for evaluation. Of these, 12 were withdrawn at the manufacturers' request. The remaining 53 products comprise 47 insecticides (23 pyrethroids, 10 insect growth regulators, 6 organophosphorus compounds, 4 carbamates and 4 chemicals in other classes), 2 molluscicides, and 4 rodenticides. These products are at various stages of evaluation.

In view of the resurgence of vector-borne diseases and the need for pesticides to control them, problems of insect resistance are likely to arise and chemical control agents with different modes of action will continue to be required. The scope of WHOPEs should be expanded to include the full range of chemical vector-control agents for use in various ecological situations.

Experience with WHOPEs and the previous Programme has shown that, with effective guidance and administration, such a collaborative scheme can yield new, effective and safe vector-control agents or formulations. The Committee, therefore, recommends that WHOPEs be expanded to cover the safety aspects of vector-control agents for domestic, urban and rural use and agents to control household pests. The experience gained by WHOPEs in safety evaluation could also be applied to new pesticides introduced for agricultural use.

## 5. **Current research on pesticides for use in public health**

### 5.1 **Pyrethroids**

In its ninth report, published in 1985, the Committee outlined the mode of action of the pyrethroids. Since then considerable experience has been gained of their use as insecticides. As a group, they are all highly lipophilic; each compound has one of two central cores in its chemical structure which is responsible for the high biological activity. The core is either  $-\text{COOCH}_2-$  or  $-\text{CCOOCHCN}-$ . Each produces a different syndrome when toxic doses are administered to mammals: the tremor (T) and choreoathetosis (CS) syndromes, respectively. All the compounds with modified chemical structures around the core so far developed for commercial use have the same mechanism of toxicity.

There is no evidence of biological effects in insects and mammals other than those attributable to the primary mode of action. The toxicity of both types of pyrethroids is due to their affinity for and intrinsic effect on receptors or targets within the sodium channels essential for nerve conduction, resulting in a delay in the closing of the sodium-channel

activation gate. Various configurations around the core produce different delays ranging from milliseconds to seconds. *Cis*-isomers are more active and more toxic than the *trans*-form, and  $\alpha$ -cyano substitution (the second core structure) leads to longer delays in the closing of the sodium-channel gate and consequently to greater toxicity.

Being highly lipophilic, pyrethroids readily pass through cell membranes and are absorbed through the skin, by inhalation, by ingestion and by any percutaneous injection. Intrinsic toxicity, as measured after intravenous injection, can be very high, but the slower absorption of pyrethroids by other routes and their rapid metabolism by ester hydrolysis and hydroxylation mean that in practice the resultant toxicity is much lower. Systemic toxicity has not been seen in users except in one country where few precautions were taken during packaging of pyrethroids and the whole body was subjected to repeated and often prolonged exposure through soaked clothing (4).

The toxicology of eleven commercially available pyrethroids has recently been reviewed using both published literature and unpublished data from industry (5,6). Two effects were regarded as indicative of potential problems in human exposure: histopathological changes in rats and skin effects in humans. Both are considered to be due to the primary action of pyrethroids on sodium channels.

Histopathological changes occurred only when repeated near-lethal doses were administered to rats, and the changes were reversible. Probably all pyrethroids cause paraesthesia, those containing an  $\alpha$ -cyano grouping being the most active. This effect is due to local contamination and is rapidly reversible with no evidence of residual or systemic effects. These conclusions have been confirmed in guinea pigs by means of a newly developed experimental system and with an amount of pyrethroids in excess of that experienced in human exposure (7).

It can therefore be concluded that field use of pyrethroids in the recommended concentrations, with the precautions necessary for the application of any chemical, poses little or no hazard to applicators. However, to avoid discomfort, the possible need for increased skin protection should be borne in mind if insect resistance or other circumstances require the application of higher concentrations.

With frequent exposure to low concentrations of pyrethroids (as from food or by skin absorption from handling of impregnated bednets), the risk of toxicity of any kind is extremely remote. Any pyrethroid reaching the systemic circulation will be metabolized rapidly to much less toxic metabolites. The same applies to exposure of crew and passengers during aircraft disinsection.

Thus, although they have a high intrinsic toxicity, the pyrethroids present little hazard to human beings exposed by the usual routes. The ratio of insect to mammalian toxicity is high. The primary interaction with sodium channels is a reversible reaction. If symptoms appear after exposure,

recovery occurs promptly once the circulating concentration falls. Toxicologically, these compounds have a useful characteristic – the production of skin paraesthesia – which provides an early indication of exposure.

## 5.2 ***N,N*-Diethyl-3-toluamide (deet)**

Deet has been extensively used for many years as an insect repellent. Its toxicity for experimental animals is low (8) and it is rapidly metabolized (9). However, a recent report from the Communicable Diseases Center in the USA (10) reviewed cases of poisoning, sometimes fatal, following the use of deet. With a single exception from a bizarre exposure, all were in children after exposure which would not be considered excessive for adults.

Another recent study (R.D. Verschoyle et al., unpublished observations) showed that deet is roughly six times as toxic to young rats (11 days old) as to adult rats (50 days old); female rats were found to be slightly more sensitive than males (25 days old). At doses of 1-3 g/kg of body weight deet caused ataxia in adult rats, associated with a spongiform myelinopathy largely confined to the cerebellar roof nuclei. Central nervous system depression and hyperexcitability were also observed. Neuropathological and electrophysiological tests suggested that these effects were reversible within a period of 3-5 days.

On the basis of these and other data, and taking into account the extensive use of deet over many years with few reported toxic effects (except occasional dermatitis), the compound is considered safe for adults, except following extreme exposure. Since children appear more sensitive, it is recommended that their skin exposure be kept to a minimum whenever possible and that deet should be applied to their clothing, rather than to their skin.

In addition, it would seem prudent to keep exposure to a minimum when using mixtures, such as deet and pyrethroids, with neurotoxic activity at high dosage, particularly when mechanisms of toxicity are unknown. A study of possible interactions between deet and permethrin would be useful. The Committee also recommends early consideration of deet and other insect repellents for inclusion in the Environmental Health Criteria Series, produced by IPCS.

## 5.3 **Chemical larvicides applied to drinking-water**

Temephos has been in use for the control of mosquito larvae (*Aedes aegypti*, *Culex* spp, and *Anopheles* spp) in drinking-water since the early 1970s. It has been useful in the control of dengue and dengue haemorrhagic fever, malaria and filariasis. The only complication has been the appearance of larval resistance in some areas. This makes it necessary to consider what other larvicides could safely be added to drinking-water. Methoprene has already been recommended for the purpose (11).

The Committee considered permethrin and triflumuron as candidate materials. The toxicity of both compounds is low. As already stated, the mode of action of permethrin is known and the effects of even large dosages are reversible. It is considered safe for addition to drinking-water at a recommended level of 15 µg of active ingredient per litre.

The addition to drinking-water of triflumuron cannot be recommended, since it is a substituted urea. Some substituted ureas are diabetogenic or neurotoxic in animals, while others have no such adverse effects. Some, for unknown reasons, show adverse effects in one species and not in another. It would be unwise to add triflumuron to drinking-water until further study has resulted in a better understanding of the mechanisms involved. The same applies to diflubenzuron.

#### 5.4 **Biological control of vector larvae**

Mammalian safety aspects of the biological control of vectors were considered in some detail in the Committee's ninth report. Since then, both *Bacillus thuringiensis* H-14 and *Bacillus sphaericus* have come into operational use. Research into the genetic manipulation of the bacteria has increased, particularly regarding the possible incorporation of the gene responsible for toxin production into other organisms, such as blue-green algae or other bacteria. Safety evaluation of these mutants is in progress, but none is yet approaching operational use.

The Committee reviewed the recommendations made at its last meeting and found that in most respects they were still valid. However, much evaluation work has been done on *B. thuringiensis* H-14 since all the safety tests were passed. As a result, hundreds of thousands of litres of formulations are now applied annually to water for the control of blackfly larvae in Africa, and for the control of nuisance mosquitos in China, France, Germany, the United States, and a number of other countries. Some of the waters to which these formulations have been applied have undoubtedly been used for drinking purposes, especially in Africa, and no adverse effects on those who applied them, the inhabitants of the river banks, or the environment have been reported. In view of this, the recommendation (II) that only asporogenic forms of *B. thuringiensis* H-14 should be applied to drinking-water for mosquito control may be unduly restrictive, provided that properly designed formulations are used.

Thorough safety evaluation of mutant bacteria will be essential whenever one of them appears effective enough in the laboratory against insects or their immature stages for field trials to be contemplated. In particular, where a strain may produce its own or an introduced toxin with heightened biological activity, extensive safety evaluation both of the organism and of its isolated toxin must be carried out.

Some means will have to be found of authoritatively assessing the safety of mutants for humans and other forms of life; any future expert committee

that considers this topic will need to include people with the relevant expertise, e.g. in genetics and microbiology.

## 6. **Aircraft disinsection**

International air traffic has increased so much that it may be contributing significantly to the rapid spread of human, veterinary and agricultural vector-borne diseases throughout the world. Vectors may infect people on the flight or people in the places it serves where the disease they carry may have been hitherto unknown (12). If the ecological conditions in places where the aircraft stops are favourable, the vectors may become established and spread the disease in the surrounding area.

The potential transport of vectors of human diseases in aircraft has been of serious concern to WHO expert committees since 1949. The characteristics of an aerosol suitable for aircraft disinsection, the Standard Reference Aerosol, to which candidate aerosols could be compared, were defined in 1957. Subsequently, aerosol application of resmethrin, bioresmethrin, *d*-phenothrin or permethrin (*cis/trans* ratio, 25/75), each with 2% active ingredient in dichlorodifluoromethane (Freon 11) and trichlorofluoromethane (Freon 12) (1:1), has been recommended for aircraft disinsection, either before take-off (the “blocks away” method) or on arrival. There has been no evidence that exposure to pyrethrins or pyrethroids, combined with a synergist such as piperonyl butoxide, has constituted a toxic hazard to passengers or crew of contaminated foodstuffs in passenger cabins and cargo holds.

The use of chlorofluoromethanes as aerosol propellants, as in the Standard Reference Aerosol, is now questioned on environmental grounds, and industry is being encouraged to seek satisfactory alternatives. The use of these propellants could be avoided by increased use of residual treatment of aircraft.

Studies carried out in New Zealand in collaboration with WHO showed that the residual spraying of the interior of aircraft was effective and compatible with normal aircraft maintenance procedures. Residual treatment with permethrin was recommended by the Committee at its ninth meeting in 1985 as having a wide toxicological safety margin. Recommendations on procedures for aircraft disinsection, including residual treatment, were subsequently published (13); they called for the use of permethrin at the rate of 0.2 g of active ingredient (a.i.) per m<sup>2</sup> on exposed surfaces of the aircraft cabin and cargo holds and at the rate of 0.5 g a.i./m<sup>2</sup> on the floor covering in the passenger cabin.

These procedures can be carried out under direct supervision in the absence of aircrew, passengers and foodstuffs. The flight deck and some surfaces in the cabin that are routinely cleaned are treated with 2% permethrin aerosol. The insecticide usually remains effective for up to

eight weeks, but retreatment can be carried out at shorter intervals to fit in with aircraft maintenance procedures.

As residual treatment with permethrin is not accepted for aircraft disinsection in some countries, the Committee felt that other pyrethroids should undergo safety evaluation if shown to be effective against vectors. Most pyrethroids would probably be acceptable. Residual treatment should be applied to cargo containers as well as the cargo hold. The Committee recommends that pyrethroids other than permethrin be investigated for residual treatment of aircraft.

In view of the possibility that vector resistance to pyrethroids may develop, further work on alternative insecticides for residual treatment should cover compounds such as bendiocarb, which is already recommended for cockroach control in aircraft (14).

## 7. **Exposure of the public to pesticides**

### 7.1 **Use of pesticides by untrained people**

Much attention has rightly been paid to preventing health hazards from pesticides for people exposed occupationally to highly toxic products. Training of pesticide applicators in the use of protective measures has been given priority, although the recommended procedures are not always followed.

In some countries, people who need to use pesticides of substantial toxicity for professional purposes are permitted to purchase them only after undergoing training in their use and receiving a licence. Less toxic pesticides may be purchased by untrained people. It is recommended that the practice of restricting the availability of highly hazardous pesticides be adopted by other countries.

There remains a group of untrained people who use pesticides either in the home or in domestic gardens. In recent years, registration authorities in developing countries have sought guidance on possible criteria for the registration of pesticides for household use, particularly with a view to protecting the very young, the very old and the sick, who may be more susceptible.

FAO is now preparing guidelines on the registration of household pesticides. The Committee has commented in the past (11) on the safety aspects of the use of impregnated bednets, fumigation mats and mosquito coils, and now feels that certain principles can be laid down to ensure that no hazard to any exposed person should arise in the recommended use of any household pesticides, as defined below. The Committee feels that similar criteria should be established for the registration of chemicals for use in home gardens, together with a code of conduct on the use of chemicals in domestic gardening and small greenhouses. The toxicological problems here differ only in degree from those of smallholders or

part-time farmers, for whom any type of training in the use of chemicals is rare.

## 7.2 Principles for risk management of household pesticides

Household pesticides can be defined as pesticide formulations intended for the control of common household pests by the occupants of a dwelling or for chemical treatment of household material, such as wallpaper, bednets or curtains, in or around a dwelling and conforming with the general provisions set forth below. They do not include formulations designed for household pest control by authorized pest-control personnel only.

Household pesticides are marketed in a variety of different formulations, such as baits, powders, sprays or aerosols, in solid form as coils or fumigation mats, incorporated into plastics or animal collars, impregnated into fabrics, or incorporated into paints or varnishes. The potential hazards presented by each of these forms must be considered, to ensure that the forms or concentrations present no hazard in normal use.

All formulations should as far as possible be available in a concentration in which dilution is unnecessary and should in any case be in Class III (slightly hazardous) of the WHO Recommended Classification of Pesticides by Hazard (15) and, as applied, should conform to the criteria for inclusion in Table 5 of that Classification (products unlikely to present acute hazard in normal use). Important exceptions are the rodenticides, where each product must be considered individually with special attention to species susceptibility.

Active materials and formulated products for household use should conform to the specifications for pesticides used in public health (3), published by WHO, or those for agricultural pesticides, published by FAO, as applicable. WHO is also preparing guideline specifications for some household pesticides. Good-quality standards should also be required for solvents and dispersion devices if they make up part of the product.

The following general provisions should be considered before a pesticide is registered for household use:

- (a) Packaging should be firm, reclosable and so designed that the pesticide can be applied directly from the package. When a package is in a form in which a child might be able to get at its contents, its size should be such that the child could consume the whole contents without adverse effects. This is especially important in the case of rodenticides.
- (b) The label should state what the product is and the pests against which it is effective, and give clear directions for use. All the information should be in local languages or dialects. The label should not be misleading and should not state that the contents are harmless to humans.
- (c) The date of manufacture should always be printed on the label.

Registration authorities may require an expiry date, appropriate to local storage conditions, to be added.

- (d) The label should carry a specific and prominent warning against transfer of the contents to another container.
- (e) Any precautions that are needed, including where applicable the prevention of contamination of food, should be easy to carry out and very simply expressed.
- (f) Disposal of used containers, even with considerable residues of pesticide, should not require special precautions, so that they can be taken away with normal domestic refuse.
- (g) A person handling a household pesticide should not need to wear any type of special protective clothing.
- (h) The flammability, explosive potential and corrosiveness of solvents used in household pesticide formulations might present a greater hazard than the toxicity of the pesticide itself. The precautions needed to prevent the product catching fire or exploding should therefore be clearly indicated on the label.

The Committee recommends that these general provisions should be brought to the attention of the FAO Panel of Experts responsible for drafting guidelines for registration authorities. It considers that household pesticides that conform to these provisions will not present any significant hazard to health for any susceptible group, provided that they are used in accordance with instructions. Misuse of pesticide formulations cannot be prevented by registration or labelling procedures, but householders must be taught to take the same care with them as they do with any other solvents, cleaning agents and medicines that are used in the household; this includes keeping them away from children.

### 7.3 Disposal of used pesticide containers

In the Committee's ninth report (*II*), it was recognized that decontamination procedures had been laid down for only a few compounds and it was recommended that governments should consider introducing economic incentives to ensure safe disposal of metal pesticide containers.

Since that report, both WHO and FAO have received information indicating that little interest has been shown in developing new techniques for the disposal of metal and other pesticide containers. It is widely known that in many countries they are regarded as useful for storage purposes, and that food and drink for human and animal use are often stored in them.

The Committee therefore considers that a different approach is now required and that containers of pesticide formulations designated as slightly hazardous or unlikely to present acute hazard in normal use (Class III, Tables 4 and 5), in the WHO Recommended Classification of Pesticides by Hazard (*15*), could be reused under certain conditions.

Adoption of the following principles and practices is recommended:

- (a) Decontamination (for reuse) of containers made of materials such as polyethylene that preferentially absorb the pesticide should not be permitted for any pesticides falling into Hazard Classes I and II (extremely hazardous, highly hazardous, or moderately hazardous), regardless of formulation.
- (b) All pesticide containers should be permanently labelled or embossed: "Not for use for food, drink or animal feed".
- (c) Containers that have held only pesticide formulations in Hazard Class III, *except* for polyethylene containers of formulations in Hazard Class III based on an active ingredient in Hazard Class I or II as described in (a) above, should be labelled as follows: "This container may be reused for purposes other than storage of food, drink or animal feed, but only after its contents have been disposed of safely, the container completely refilled with water and allowed to stand for 24 hours, and the whole process repeated twice. After this serial washing, obliterate this label".
- (d) The containers of formulations in Hazard Class Ia, Ib, or II, as well as polyethylene containers of formulations in Hazard Class III based on an active ingredient in Hazard Class I or II, should carry an additional permanent label or embossed warning "When emptied and drained this container must be destroyed". The method recommended for safe disposal should be described.

A summary of these procedures is given in Table 1.

The Committee is referring these recommendations to FAO in the hope that new studies will begin, by collaboration between WHO, FAO, and industry, to devise new and simple methods for decontaminating containers of pesticides in Hazard Classes Ia, Ib, and II. In view of the hazards associated with what appears to be the inevitable reuse of such containers, the Committee would like to see the concept of product stewardship by industry extended to include decontamination of containers of all hazard classes of pesticides, on the lines of its previous recommendations (*II*).

Table 1

**Labelling of pesticide containers**

Containers of Hazard Class III and less hazardous formulations (except polyethylene containers of chemicals in Hazard Classes Ia, Ib, or II, regardless of formulation)

*Permanently labelled or embossed:*  
"Not for use for food, drink or animal feed."

*Labelled:*  
"Container may be reused for purposes other than storage of food, drink or animal feed, but only after its contents have been drained into a safe place, the container completely refilled with water and allowed to stand for 24 hours, and the process repeated twice. After this serial washing, obliterate this label."

Containers of formulations in Hazard Classes Ia, Ib and II, as well as polyethylene containers of formulations in Hazard Class III based on an active ingredient in Hazard Class I or II

*Permanently labelled or embossed:*  
"Not for use for food, drink or animal feed."  
*Warning.* When emptied and drained, this container must be destroyed."

Details of a method of safe disposal should be added.

## 8. **Classification of pesticides**

The Committee has considered the evolution of the WHO Recommended Classification of Pesticides by Hazard on several occasions in the past and notes that a history of the Classification has been published (16). The Classification has been adopted by a large number of countries, either in its original form or adapted to their needs, and forms an integral part of the FAO International Code of Conduct on the Distribution and Use of Pesticides (1). It is emphasized that the prime function of the Classification is to prevent acute intoxication of humans by pesticides, and there is no doubt that the Classification is needed and that the guidelines (15) should continue to be developed.

In so far as the Classification depends on LD<sub>50</sub> values as a starting-point, it is based on animal experiments, and there is a marked movement towards reducing the number of animals used to obtain the relevant data. The current trend in regulatory toxicology to try a simple dosage first at a level of 2000 mg/kg of body weight of the animal, and to carry out further tests only if it appears that the LD<sub>50</sub> is below that level, may lead to minor adjustments in the Classification, but should not reduce its usefulness in any way.

On the other hand, it is difficult to see how testing in animals could be dispensed with in the foreseeable future. Laboratory tests on individual cell-lines or other *in vitro* systems are useful for defining a particular

toxicological property but are not so reliable for quantitative estimations, so that it is difficult to extrapolate a toxicologically safe dosage from the results. In addition, they often rely on effects at cellular level rather than the disruption of a physiological system. They do not take into account what pathways the toxicants follow in the body after their absorption or of the effects of their metabolites in the animal as a whole.

The Committee recommends that the basis of the Classification should be unaltered at present and urges users of the Classification to consider other effects of pesticides. The cross-references in the “Remarks” column of the tables in the Guidelines to WHO/FAO data sheets on pesticides, Health and Safety Guides, and the Environmental Health Criteria Series may be useful in this regard. The guidelines should continue to be revised at 2-year intervals.

## 9. **Education and training**

Education and training in the safe use of pesticides are needed primarily for the prevention of misuse of pesticides and resulting intoxication. These objectives must always be kept in mind when course content is being determined.

The level of training will vary according to the background and education of the participants. There is often a tendency to include too much detail for the length of the course, without considering participants' preconceptions when they enter it. Courses in the safe use of pesticides should emphasize the need to reduce exposure, and outline the basic concepts that underlie practical recommendations on safe use.

This brief recapitulation of what has often been said already is necessary because much money has been wasted through lack of attention to the relevance and practicability of courses. If courses are to be effective, those who take them should be of similar educational background, and should be in a position to apply the lessons learnt within a reasonable period of time. In international courses adequate knowledge of the languages of the course will also be essential.

Each course should have three phases in its organization: a preparatory phase, the course itself and evaluation.

- (a) During the preparatory phase potential participants should be asked to define the problems that they face. Their replies should be taken into account in the way the course is presented.
- (b) During the course itself it has been found useful in some cases to put the lessons taught into immediate effect. This applies especially to “train the trainers” courses, which can be followed by a course run by a trainer for a group of intended trainees, under the supervision of those presenting the original course. This has proved to be instructive for both the “trainers of the trainers” and their pupils.

- (c) The course is often evaluated on the basis of a questionnaire, which should be anonymous and comprehensive. The questions should be designed to determine whether the course objective has been achieved as a whole or in part, and whether the methods used have been effective. While the questionnaire may be completed at the end of the course, evaluation is not complete until the results of the course have been followed up some months later.

There is a wide variety of courses on safe use of pesticides, many of which are sponsored by international bodies or national institutes. The Committee recommends that a study should be made of those already evaluated in order to single out principles that can be applied by the designers of future courses and determine the pitfalls to be avoided. The WHO Multilevel Course on the Safe Use of Pesticides, which has a number of novel features to make it more relevant to differences in conditions in different countries, needs updating and such a study should be a preliminary part of the updating process.

## 10. **Poisoning by pesticides**

### 10.1 **Advances in monitoring of exposure to pesticides**

Monitoring of human exposure to pesticides is designed to stop exposure reaching a point at which poisoning might occur. Biomonitoring is defined as determination of dose-effect relationships in humans by means of biochemical measurements in accessible body fluids (17).

Toxicity following exposure to a chemical starts when the chemical itself or a bioactivated form of it reaches the primary target. Changes that occur in that target may lead to signs or symptoms of toxicity (18). Dose-response relationships relating exposure to toxic effects are usually difficult to interpret, but they provide a useful operational concept. Recent research has been focused on measuring parameters indicating the internal dose of the chemical and/or its transformation products. Methods include measurement of the concentration of the chemical or its metabolites in urine or in blood. For electrophilic chemicals, the measurement of adducts resulting from their reaction with the nucleophilic centre in proteins (e.g. haemoglobin) or nucleic acids (DNA) provides information on the reacting dose reaching the target (19). This quantitative approach allows calculation of the ratio of the applied dose to the reacting dose. This will make possible more rational extrapolations from one species to another. Furthermore, the biomonitoring of internal doses is possible for a relatively long time after the end of exposure and is becoming an essential component of modern epidemiology. This new approach might provide quantitative data on biochemical effects that are proportional to internal dose, for example on erythrocyte acetylcholinesterase or plasma cholinesterase following exposure to organophosphorus compounds or carbamates, or even on the consequences of oncogene activation (20).

These results may be achieved once targets have been determined and the mechanisms of toxicity are understood. The Committee notes this direction of research with interest and wishes to be informed of further developments as they occur, with a view to using some of the methods evolved.

## 10.2 Epidemiology of acute pesticide poisoning

There is a paucity of reliable epidemiological data on the extent of acute pesticide poisoning. In 1972, on the basis of a theoretical model, a WHO Expert Committee made the first global estimate of the number of cases of acute pesticide poisoning (21). This indicated that the problem was large and required urgent attention. Data supporting the model were subsequently obtained through studies in Indonesia, Malaysia, Sri Lanka and Thailand, and further estimates were made which tended to confirm the earlier estimate. It is clear that the problem of acute pesticide poisoning is largely a problem of the developing world, since it is relatively well controlled in developed countries.

The extent of the problem of acute pesticide poisoning as a major health concern was highlighted in the Sri Lankan study (22). It was found that during the year of the study, 982 deaths from acute pesticide poisoning occurred in State hospitals. This figure strikingly demonstrates the public health importance of the problem as it was almost twice as high as the total number of deaths in the same hospitals due to malaria, poliomyelitis, whooping cough, diphtheria and tetanus, the traditional killers in the developing countries.

The studies in developing countries found that approximately two-thirds of all acute pesticide poisonings were suicide attempts and approximately one-quarter were accidents (both occupational and non-occupational); in the remaining cases the cause was not defined. Pesticides are often used to commit suicide in these countries because these hazardous compounds are readily available to the public, whereas in developed countries, the more toxic the product, the more restricted its availability.

In view of this situation, urgent intervention is required in many countries to restrict the availability of highly hazardous pesticides. Although many developing countries have passed legislation to control pesticides, enforcement is often inadequate or nonexistent. Experience in developed countries has shown that restricting the availability of highly hazardous pesticides, together with proper packaging and labelling, significantly reduces the incidence of pesticide poisoning. Wider use of the WHO Recommended Classification of Pesticides by Hazard, within the framework of the FAO Code of Conduct on the Distribution and Use of Pesticides, should be helpful in this regard.

The Committee recommends the urgent introduction of intervention programmes, in countries where they do not already exist, to reduce acute pesticide poisoning. In any control programme, all the parties involved

need to collaborate to find a solution. Governments, the agrochemical industry, the community, scientists and international agencies all have a role to play. Governments should undertake studies of the prevalence of pesticide poisoning similar to those mentioned above, in order to determine the scale of poisoning and define clearly where intervention in the distribution of pesticides is needed.

### 10.3 Treatment of pesticide poisoning

In order to treat victims of pesticide poisoning, medical personnel need up-to-date and reliable information and it must be readily available whenever a poisoning occurs. Where they exist, poison control centres provide such information on a round-the-clock basis. Such centres are needed in every country. The Committee notes that WHO is preparing guidelines on poisons control and is implementing a project to strengthen the ability of Member States to deal with all types of poisoning through the provision of a poisons information package, INTOX, both in hard copy and in computerized form. The package is available in English, French and Spanish, and contains information on the physical, chemical and toxicological properties of pesticides, how to analyse them, and how to diagnose, treat and prevent poisoning. The package describes a methodology and format for collecting and storing local data on commercial products containing pesticides as well as a format for reporting and recording cases of pesticide poisoning. Furthermore, a handbook on poisoning is being prepared, both for primary health care workers and for doctors who have no access to hospital facilities, on how to prevent and manage poisoning cases (23). In addition, a manual on analytical toxicology (24), describing simple analytical techniques for detecting and measuring pesticides and other poisonous substances in body fluids, has been prepared for use in hospital laboratories.

There are very few specific antidotes for the treatment of pesticide poisoning and even those that exist are not readily available in adequate quantities in some developing countries. The Committee is of the opinion that antidotes and other drugs essential for the treatment of victims of pesticide poisoning should be available whenever and wherever pesticides are used.

No major advances in the treatment of pesticide poisoning have occurred in recent years. The notes on treatment of poisoning by organophosphorus, carbamate and organochlorine insecticides, anticoagulant rodenticides and paraquat, which were published as an annex to the Committee's ninth report (11), were reviewed and a revised version is given in Annex 1.

The Committee notes the project at present being conducted by the International Programme on Chemical Safety (IPCS) and the Commission of European Communities to evaluate the clinical efficacy and field use of antidotes. The results of these evaluations as they relate to pesticides will

be published in monographs devoted to specific chemicals or to specific antidotes and other agents used for treatment. Since the majority of pesticide poisoning cases occur in developing countries, the strengthening of their research capabilities in this field should be a priority.

The Committee further observed that the work of the IPCS in that regard could provide a basis for establishing an international mechanism for collecting and analysing standardized information on exposure to pesticides and their observed toxicity, including possible long-term sequelae.

## 11. **Conclusions and recommendations**

The main conclusions and recommendations of the Expert Committee are as follows.

### 11.1 **General**

1. Chemical pesticides will continue to play a dominant role in disease vector control in the foreseeable future.
2. The pyrethroid insecticides currently in use seem to be remarkably free from adverse effects. Their local effect, paraesthesia, is of short duration and completely reversible. If normal precautions are taken, pyrethroids pose little or no hazard either to sprayers, or to the general public as a result of minor exposures from treated bednets or vaporizers.
3. Deet in high doses is a neurotoxin but its application to adults in amounts normally required to repel insects is unlikely to cause problems. However, children appear to be more sensitive and application to the skin should be limited and reinforced by application to clothing.
4. Permethrin added to drinking-water as a larvicide at a concentration of 15 µg/l is considered safe. Triflumuron and other substituted urea larvicides should not be added to drinking-water until the possibility of the diabetogenic side-effect found with some substituted ureas has been excluded.
5. The testing of pyrethroids other than those already recommended for aircraft disinsection should be encouraged. It is recommended that residual treatment of the cabin and cargo hold should replace aerosol dispersion in the cabin during flights. The problem of insects surviving in containers can be solved by residual spraying of cargo containers both inside and out.
6. Non-absorbent containers of active ingredients of pesticides and formulations in Hazard Class III can be reused, after a serial washing procedure, for purposes other than storage of food, drink and animal

feed. The recommended labelling is indicated in the body of the report (section 7.3).

7. In some countries, the problem of acute pesticide poisoning is so serious that urgent action is required. Further epidemiological studies should be undertaken to evaluate the effectiveness of intervention measures. International agencies should help countries implement programmes for this purpose.
8. Member States should be encouraged to strengthen existing poison control centres or establish such centres where they do not yet exist, in order to have information available on poison control at all times, including information on how to deal with pesticide poisoning.
9. Every effort should be made to provide adequate medical care for the victims of pesticide poisoning. Antidotes should be available wherever they may be needed.

## 11.2 Recommendations to WHO

1. Collaboration between WHO, FAO, UNEP and ILO should be strengthened to ensure that their activities in relation to the safe use of pesticides are complementary and do not overlap.
2. The safety aspects of the WHO Pesticide Evaluation Scheme (WHOPES) should be expanded to include agents for controlling domestic, urban and rural vectors and household pests.
3. The guidelines to the WHO Recommended Classification of Pesticides by Hazard should continue to be updated every two years.
4. WHO should continue to play a leading role in the toxicological evaluation of pesticides in regard to human exposure, or for registration and control purposes necessitated by provisions of the FAO International Code of Conduct on the Distribution and Use of Pesticides, including the "Prior Informed Consent" procedure.
5. Courses in the safe use of pesticides held by other organizations and institutes and subsequently evaluated should be studied to determine the factors influencing their success. The WHO Multilevel Course on the Safe Use of Pesticides should then be brought up to date accordingly.
6. As the capacities of countries' poison control centres are strengthened, an international mechanism will be needed for collecting data on exposure to pesticides and other toxic chemicals in a standardized and comparable form and analysing all aspects of any toxicity observed, including possible long-term sequelae.
7. In response to requests from Member States for information on ways of ensuring that pesticides used in the home or garden pose no hazard, certain provisions for household pesticides have been outlined. WHO is requested to bring these provisions to the attention of FAO for

consideration for inclusion in the guidelines for registration authorities now being prepared.

8. WHO is requested to bring the Committee's recommendations on the decontamination and reuse of pesticide containers to the attention of FAO and the manufacturing industry, with a view to establishing collaborative efforts to solve the problems of reuse of containers.

### 11.3 Recommendations for future research

1. A simple toxicological study should be carried out to test for synergism between deet and permethrin.
2. Research on biomonitoring that may lead to new methods for measuring exposure to pesticides and its effects should be pursued.

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## Annex 1

# **Treatment of poisoning due to organo-phosphorus, carbamate, and organochlorine insecticides, anticoagulant rodenticides, and paraquat**

Successful treatment of pesticide poisoning depends on the rapid and simultaneous application of measures for: (a) alleviation of life-threatening effects; (b) removal of non-absorbed material; and (c) symptomatic and/or specific treatment.

### **1. The alleviation of life-threatening effects**

For the removal of secretions and maintenance of a patent airway, place the patient in the prone position with head down and to one side, the mandible extended and the tongue pulled forward. Clear the mouth and pharynx with a cloth or by suction. Use an oropharyngeal or nasopharyngeal airway or endotracheal tube if airway obstruction persists. Artificial ventilation should be applied if required. Mouth-to-mouth respiration is to be avoided when it is suspected that the patient has been intoxicated by mouth, because vomited material may contain dangerous amounts of toxic substances.

### **2. The removal of non-absorbed material**

Absorption of toxic material present in the gut or on the skin may continue for days. The condition of intoxicated patients who have become free of symptoms may deteriorate when newly absorbed toxic material reaches the bloodstream. When intoxication has occurred by mouth, gastric lavage is imperative. If the clothing or exposed skin is contaminated by pesticide, the clothing must be removed and the skin washed with soap and water for at least 10 minutes. Contamination of the eyes is treated by irrigation of the conjunctiva with water for 15 minutes.

### **3. Symptomatic and/or specific treatment**

#### ***Intoxication with organophosphorus compounds***

On the appearance of signs of systemic poisoning, both atropine and reactivators must be given parenterally.<sup>1</sup> If possible, blood samples should be taken for cholinesterase determinations before and during the treatment.

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<sup>1</sup> When symptoms occur before medical attention is available, atropine with or without obidoxime may be given by intramuscular injection. For this purpose, automatic injectors loaded with atropine sulfate or with a combination of atropine sulfate and obidoxime chloride are available. For pharmaceutical reasons, the combination of atropine and a pralidoxime salt is impracticable.

Persons with manifest peripheral symptoms or signs should be treated with 2-4 mg of atropine sulfate and 1-2 g of a soluble salt of pralidoxime every 6 hours, or 250 mg of obidoxime chloride every 6 hours<sup>2</sup> by slow intravenous injection (adult doses). More atropine may be given, depending on the severity of the intoxication and the response to the previous dose. After the administration of oximes, less atropine may be required. Oxime therapy should be continued until clinical improvement and/or a sustained increase in cholinesterase activity is observed. Even if the patient comes for treatment 36 hours or more after intoxication, oxime therapy may be effective.

In cases of severe intoxication, 4-6 mg of atropine sulfate should be given initially to adults, followed by repeated doses of 2 mg or as much as is required to maintain full atropinization. Whenever possible, this treatment should be given concurrently with measures for the alleviation of life-threatening effects and the removal of non-absorbed material. The patient's condition – including respiration, convulsions, blood pressure, pulse rate, lung secretions and salivation – should be carefully observed as a guide to further administration of atropine; lung secretions and pulse rate are the best signs against which to judge atropine dose. Initially atropine may have to be given at intervals of 5-10 minutes. Every dose of 2 mg should give a short-lasting improvement of respiration and reduction in cyanosis and convulsions. Tachycardia may occur and a watch must be kept on the pulse rate in order to prevent over-atropinization, although this is not as dangerous as under-atropinization. Cases are described in the literature in which several hundred milligrams of atropine have been given during the first 24 hours. Continuous intensive observation of patients is essential since symptoms may recur and, if treatment is not given, death may result. In every case, observation should be maintained for at least 72 hours after initial improvement. In severe poisoning, the period of observation should be extended to one week. Deaths have been reported several days after poisoning, owing to premature cessation of atropine therapy.

In moderate or severe poisoning, 5-10 mg of diazepam (adult dose) should be given intravenously and repeated if necessary, to reduce the severity and frequency of muscle fasciculations and convulsions. In mild poisoning, oral diazepam may be helpful in relieving anxiety.

### ***Intoxication with carbamates***

The signs and symptoms of carbamate poisoning resemble those of organophosphorus poisoning but, since the features of carbamate poisoning disappear comparatively rapidly, atropine treatment may not be necessary by the time the patient reaches a place where the antidote is

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<sup>2</sup> Attention is drawn to the fact that liver damage has been associated with high doses of obidoxime.

available. In cases of poisoning in attempted suicide, 1-2 mg of atropine sulfate (adult dose) may be given intravenously, and the dose repeated as necessary. Care should be taken to avoid overdosage in cases of carbamate poisoning, especially in children. Oximes should not be given.

### ***Intoxication with organochlorine compounds***

There is no specific antidote. Treatment is aimed at controlling the symptoms, especially hyperactivity and in some instances convulsions. Artificial ventilation may be required. Anticonvulsant treatment with barbiturates, diazepam, or paraldehyde should be given in sufficient dosage to calm the patient and prevent convulsions.

Blood analysis for organochlorine levels may be used to confirm the cause of poisoning, but, since this is at present a lengthy and highly specialized procedure, treatment should never be deferred pending the result of a laboratory test.

### ***Intoxication with anticoagulant rodenticides***

The principal method of managing intoxication by conventional or second-generation anticoagulant rodenticides is administration of phytomenadione (vitamin K<sub>1</sub>). After blood samples have been taken for differential diagnostic tests, including the measurement of prothrombin levels, phytomenadione (vitamin K<sub>1</sub>) in a dose of 5-10 mg should be given three times on the first day of treatment irrespective of symptoms. The vitamin should be diluted with an injectable 5% solution of dextrose or sodium chloride and given intravenously, preferably by infusion. Intramuscular administration of smaller doses of phytomenadione should be continued until the prothrombin time has reached normal. In addition to phytomenadione, a seriously ill patient should initially be given a transfusion of carefully matched whole blood (as little as 50 ml may be effective); transfusions may be repeated daily until the patient's prothrombin time has returned to normal. Prolonged observation of patients affected by second-generation anticoagulants (coumarin derivatives) is required because these compounds are metabolized slowly and repeated therapy may be indicated. In any event, the progress of the patient should be assessed by monitoring the prothrombin time of blood samples taken at least twice a day; monitoring should continue until a return to normal is clearly established. The coumarin derivatives are susceptible to interaction with some drugs.

### ***Intoxication with paraquat***

No antidotes currently exist and management essentially relies upon the use of adsorbents to prevent absorption from the gut and upon the removal of absorbed paraquat from the body, although these measures are rarely effective in severe poisoning. One litre of a suspension of fuller's earth (about 300 g/litre) or bentonite (about 70 g/litre) should be administered orally as soon as possible and repeated in doses of 200-500 ml every two

hours for several days. A cathartic agent such as magnesium sulfate should be given at the same time to avoid intestinal obstruction due to the adsorbent. Activated charcoal may be more effective in adsorbing paraquat and should be used if it is available. In an emergency, use of ordinary soil may be beneficial if these adsorbents are not available. Administration of oxygen is contraindicated in acute poisoning because paraquat is more toxic in the oxygenated lung; the use of oxygen should be delayed for as long as possible.

#### 4. **Other considerations**

If a number of patients are found to be exhibiting symptoms suggestive of poisoning by a pesticide (or other chemical) without a history of exposure, the possibility of the cause being gross contamination of a food item or drinking-water, or being unrelated to any chemical, should be borne in mind.

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