Evaluating Hazards in Pesticides Use

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Used pesticide containers must be destroyed promptly by burning or burying

Regulations designed to reduce pesticide hazards must be based on evaluation of potential hazards to three distinct groups of people

ROBERT LOUIS STEVENSON in his essay "Aes Triplex" made it clear that even if it were possible to avoid all hazard, such a life would not be particularly interesting. Actually there is danger in every human activity. The very air we breathe may be laden with pathogenic organisms when we least expect it. Thus normal living requires frequent and continuing exposure to hazards of various degrees. Most well-adjusted people devote very little time or effort to concern for these mutliple hazards. Yet the "dare devil" who purposely exposes himself to increased risks is not exactly typical, and a legitimate activity of organized society is the attempt to reduce or at least to evaluate various hazards.

The U. S. Department of Agriculture was given the responsibility of assuring that all pesticides sold in interstate commerce would be adequately labeled for the safety of the consumer. Likewise the Food and Drug Administration of the U. S. Department of Health, Education, and Welfare was given similar responsibility of assuring that fruits and vegetables moving in interstate commerce would not bear dangerous residues from such pesticides.

Regulations designed to reduce hazards must be based upon a sound evaluation of such hazards and a judicious balance between the hazards of use and the benefits to be gained thereby. It is obvious that many hazards could be eliminated by a complete halt of the use of the dangerous element. The staggering annual mortality from automobile accidents could be reduced to the vanishing point by the simple procedure of stopping all automotive traffic. But, the many and obvious advantages of this mode of transportation are such that this suggestion is ludicrous. On the other hand the suggestion that all real or imagined hazards from pesticides should be eliminated by prohibiting their use actually has been advanced within the past decade. A more reasonable approach, as in the case of automobile accidents, would appear to involve careful appraisal of those "use habits" which contribute to accidents or excessive hazard with suggestions of reasonable methods for controlling them.

Three Types of Hazards

The agricultural use of pesticides involves potential hazards to three distinct groups of people, each of whom should be considered separately. First, the applicator has the heaviest potential exposure but likewise is most aware of it and, therefore, has the best chance to protect himself if he will. He has a relatively great danger of dermal exposure through drift from the spray or dust he is applying. Secondly, residents or

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transients who are in the vicinity of agricultural pesticidal operations may experience some degree of exposure either by accident or, at least potentially, by drift. This group also includes children who may find pesticide containers either full or partially empty. (It must be borne in mind that no such used container is ever completely empty.) Children playing with such containers account for a major portion of the deaths attributed to pesticides each year. Finally the consumer may be exposed to the residues of pesticides on the agricultural products he consumes. His exposure is largely limited to the oral route.

In all cases the evaluation of the hazard involved depends upon a number of factors. First is the evaluation of the degree of exposure under conditions of use. Use of an aerosol or fumigant may result in heavy potential respiratory exposure, whereas coarse wet sprays of relatively nonvolatile substances may produce negligible respiratory exposure but potentially heavy dermal exposure. Aerial application over an inhabited area produces a potentially higher degree of environmental exposure to residents of the area than does the use of a soil fumigant in an isolated seed bed though the latter may create a greater operator exposure. The use of a stable chlorinated hydrocarbon directly to the nearly mature fruit or vegetable submits the consumer to a potential exposure which is not present when the same material is applied to dormant trees though the dormant application may produce more potential environmental exposure.

Basic Toxicity

Another factor of obvious importance is the basic toxicity of the pesticide. This is frequently expressed in terms of the acute oral dosage required to produce a 50% mortality in experimental animals (LD_{50}). The shortcomings of such an index by itself should be self-evident. The actual hazards seldom involve either an acute oral exposure or experimental animals. It is perhaps not rare for children or others to drink a solution containing a pesticide, but this is hardly the typical exposure. Dermal exposures are much more common and with many materials, such as fumigants, respiratory exposures may be more common than acute oral exposures. Of course the residue problem is concerned with oral exposure but usually of a chronic rather than an acute nature. Moreover, every farmer is familiar with the fact that some pesticides are extremely specific in their action, being effective against one species and only slightly so against even closely related species. Similarly, it is difficult to predict how toxic a compound will be to man from its toxicity to any one experimental animal.

In spite of its shortcomings, acute oral toxicity may be an excellent guide to relative toxicity especially when it is based upon more than one species of animal and particularly if it is supported by more extensive data on toxicity by other routes, and by chronic studies or at least by multiple doses. Also involved and practically inseparable from toxicity is speed and degree of absorption by various routes. Under conditions of exposure that are likely to occur in agriculture, the onset of illness and progression of symptoms is likely to be more rapid following exposure to TEPP than following exposure to parathion.

A third factor in the evaluation of hazards of use is the availability and acceptability of protective devices. Undoubtedly the most important protective device available to applicators is the very clothes they wear. There is some evidence (*11*) that ordinary cotton clothing protects the sprayman from 90% or more of the DDT sprays that would otherwise contaminate his skin. Whether this degree of protection would continue if the same clothes were worn a second day without laundering is extremely doubtful. More data are needed on this and on the degree to which it applies to other compounds applied in other ways.

Evaluating Protective Devices

The evaluation of respirators as protection from pesticides has been carried out both by the manufacturers of such devices and by the USDA. Significant progress has been made in the development of devices which will protect against a broad spectrum of materials. Of course the scientists involved have recognized that efficiency in removing the material from the air stream is not enough—the equipment must be acceptable to the workman as well. Thus, air-tight goggles are not acceptable to pilots for they fog up. Protective goggles must exclude dust and yet permit ventilation.

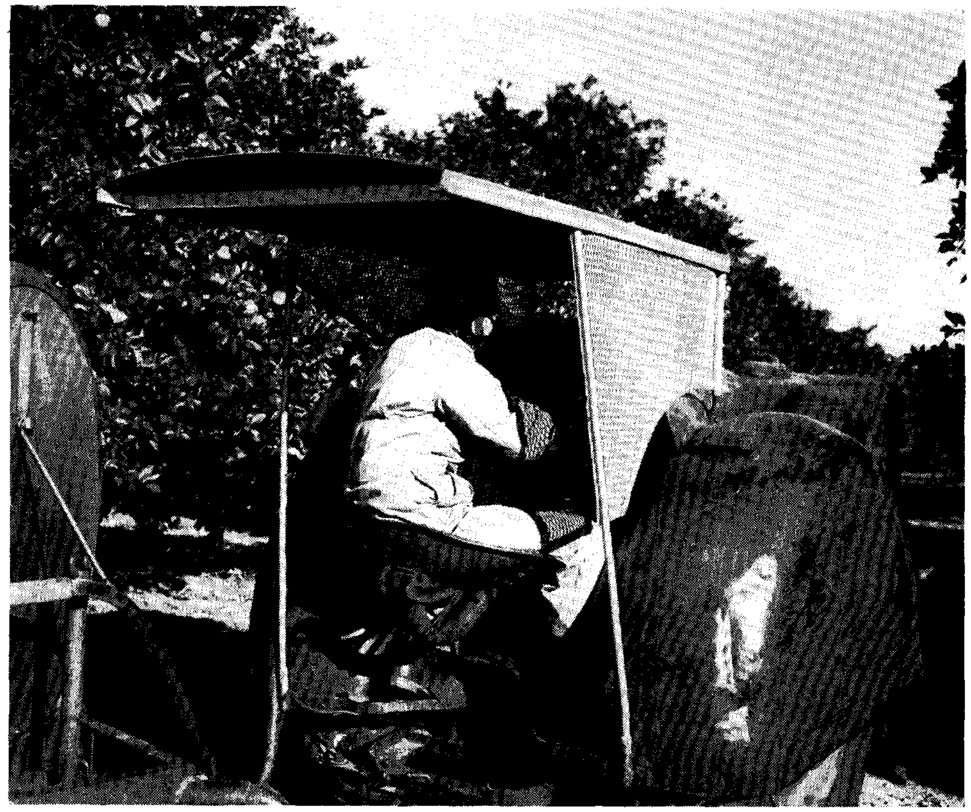
This factor of protective devices can be extended in a sense to include the wash

Any useful item, be it automobile or pesticide, requires practice of established safety procedures to avoid excessive hazards

ing and processing of fruit and vegetables to remove residues. The formerly extensive use of hot acid and hot alkali washes to remove lead arsenate residues from apples is now largely a thing of the past but there can be no doubt that handling, packing, and processing fruits and vegetables still removes a large proportion of the residues remaining at harvest. This process, of course, continues even in the kitchen.

Another factor closely related to safety devices is the selection of formulations which keep the hazard of a particular pesticide to a minimum. The introduction of "antidusting" water-wettable powders has considerably reduced the exposure during loading and mixing such powders in the spray tank. Hayes and Pearce (*6*) have mentioned several improvements of this type but point out that little has been written on this specific subject, although it is worthy of extensive consideration.

Still another factor is the actual clinical course when someone is poisoned by the material in question. Are there warning symptoms or does death follow very rapidly the first signs of intoxication? As mentioned, parathion is a little slower acting than TEPP, allowing more time for seeking and applying medical help. Are the early symptoms sufficiently distinctive to be readily recognized or are they apt to be overlooked as unrelated? It is reported that the only warning symptoms of poisoning by DNOC are lassitude, extreme thirst, and headache, which are very apt to be overlooked as normal in hot weather. Are there satisfactory antidotes or treatments available? The prompt use of atropine has undoubtedly saved victims of parathion whereas the treatment for DNOC poisoning is less satisfactory. It is readily apparent that a substance which is as noxious as chloropicrin may be less hazardous than a material of similar or lower toxicity which offers no immediate and specific warning of over-exposure.



Removable canopies on tractors help to minimize the spray drift hazard

Case I

A large proportion of fatal poisonings with pesticides occur among children who play with discarded containers. A typical case got wide newspaper publicity in March 1954. M. O. a six-year-old boy, found a gallon jug of 40% TEPP concentrate which had been abandoned in an orchard near his home. In the course of trying to open it he spilled some on his legs. By the time he got home he was in a state of collapse. Without knowing what was wrong with him his father rushed him to the doctor but the boy stopped breathing en route and the resultant lack of oxygen so damaged the brain that the boy died six days later without being able to breathe naturally again. This case also illustrates the speed of action of TEPP even when the exposure is apparently limited to the dermal route; and the importance of the first-aid principle that artificial respiration when required takes precedence over all other first-aid treatments.

Some of the techniques that are useful in evaluating health hazards are apparent in the factors already discussed. The determination of toxicity to experimental animals is a good place to begin. Even the most devoted scientist does not care to volunteer to prove the safety of an entirely new compound on himself without some evidence of its toxicity to animals. Hazelton (*7*) has presented an interesting review of the procedures used to evaluate the toxicity of a new material and Bradley (*2*) has described how hazards are controlled in the manufacturing process. The evaluation of the hazard of residues to the consumer has frequently been based upon the application of administrative judgment based on laboratory toxicity studies. Seevers (*9*) has emphasized the dangers involved in relying upon laboratory procedures. FDA has recognized this fact in their statement, regarding the fixing of residue tolerances that "where there has been extensive exposure of humans to the [pesticide] and data are available concerning any physiological or other effects on humans, a safety factor of somewhat less than 100 may be employed" (*4*). (A safety factor of 100 is used where experience is limited to experimental animals.)

Mere observation of human use experience over a period of time is not sufficient for it is quite apparent that the health of a segment of the population might be seriously impaired without associating cause and effect correctly. The recent efforts to associate epidemics of poliomyelitis with their modes of transmission should persuade a scientist that the solution to the problem cannot be arrived at simply by casual observation. Some type of controlled epidemiological study is essential. Thus Neal *et al.* (*8*) conducted a careful study of people classified as orchardists or consumers based upon their exposure to lead arsenate as an apple spray. Out of 542 orchardists, seven had a combination of clinical and laboratory findings directly referable to the absorption of lead arsenate. This was not true of any other orchardists nor of any of the 241 consumers, many of whom ate large numbers of unwashed apples. More recently Fowler (*5*) was able to compare mortality and morbidity rates in agricultural and nonagricultural areas of Mississippi and also to compare these rates before and after the introduction of chlorinated hydrocarbon insecticides into the agricultural delta. By this study he produced a forceful negative answer to the charges that exposure to such insecticides was markedly increasing the incidence of a number of common diseases.

Case II

In most cases of poisoning among spraymen the patient is aware of an unusually heavy dermal exposure. In some cases, like one described by Sumerford *et. al.,* it seems that ordinary clothing might have provided some measure of protection. R. S., a 24-year-old white man was placed in a crew to help spray an orchard on July 23, 1952. The formula included 6 pounds of 25% parathion wettable powder and 9 pounds of a 50% DDT wettable powder in 600 gallons of water and applied at the rate of 1700 gallons per acre. R. S. worked July 23 and the morning of July 24. The wind prevented further spraying until July 26. By noon that day the patient was so unbearably hot that he discarded his raincoat and respirator and worked the rest of the day with only his pants and boots as protection. He is reported to have become soaked with the spray.

After dinner he complained of "light headedness," a slight headache, and dizziness. He started vomiting and passed out several times. Perspiration was profuse, he suffered muscle and abdominal cramps, tightness in the chest, and blurred vision. After taking 0.01 grain atropine sulfate by mouth he was hospitalized at 9:00 P.M. By this time he was in a shock-like condition and disoriented.

In the hospital he was given more atropine, oxygen, and other supportive treatment. He was still very sick the next morning but gradually improved that day and was able to retain his first meal that evening. The patient was recovered sufficiently to permit discharge from the hospital on the fifth day (July 30) but was still weak and had a headache and some nausea. He started working part-time on Aug. 2 and was back full-time on Aug. 7, 12 days after the onset of symptoms. His plasma cholinesterase had dropped to 0.03Δ pH/hr. and his erythrocyte cholinesterase to 0.09Δ pH/hr. Both values are slightly less than 10% of normal.

Sumerford *et al.* (*10*) conducted a survey among people with various degrees of exposure to the organic phosphorus insecticides. Their survey included determination of blood cholinesterase activities on a monthly basis before, during, and after the season of heavy exposures. They also carefully recorded the occurrence of one or more of a list of over 100 signs or symptoms. The results indicated a significant lowering of cholinesterase activity and a corresponding increase in frequency of certain selected symptoms during the period of heavy exposure among those individuals with a known heavy occupational exposure. Those groups having less exposure had correspondingly less effect on cholinesterase or on frequency of symptoms. Those individuals simply living in an orchard area with no occupational or heavy accidental exposure showed no more effects than residents of towns completly outside the agricultural area.

Walker *et al.* (*13*) were able to recover detectable quantities of DDT and its metabolite DDE from one or more items in every meal they analyzed. The meals were selected to be typical of those obtained in the average restaurant throughout the country and avoided specialized diets. The total amount of DDT was very small in every meal, so that even if the highest values are selected from breakfast, lunch, and dinner, and combined, the total intake of DDT from such meals would be less than 0.5 milligram per day. Estimates of the minimum amount of DDT which might have adverse effects on a human have ranged from 2.5 to 5.0 milligrams per day or even higher. Such data provide interesting estimates of the exposure of the general population through consumption of foods which bear insecticidal residues. Similar data can be obtained in the case of DDT by determining the level of DDT storage in the fat of individuals with no known occupational exposure.

Determining Exposure

Exposure of the resident or transient to pesticides, simply by being in the vicinity at the time spraying takes place, is more difficult to evaluate. The most common approach to this problem is based upon the assumption that such exposure must be air-borne. Therefore, various methods of air-sampling have been tried. In so far as the basic assumption is correct, air sampling techniques rather consistently have shown the concentration of the newer insecticides to be near or below the sensitivity of chemical methods at a distance of only a few yards from spraying equipment. Even if air sampling and analytical methods were accurate at the levels encountered, there are several problems in translating such results into exposure estimates expressed in the traditional units of

A respirator and gloves should be worn when dangerous chemicals are handled

milligrams per kilogram of body weight. If dermal exposure is to be considered, are the particles so small that laminar flow will carry them around the body rather than impinging them on the skin? Even assuming that all the particles are such that they will impinge upon the skin, the conversion of air concentration in micrograms per liter, through a time factor as well as the space factor, to end up in milligrams per kilogram of body weight is at best very hypothetical.

The more common conversion assuming the exposure to be chiefly respiratory is much more satisfactory. But even such a conversion involves estimates of the tidal air volume breathed in a unit of time under conditions of activity expected to be encountered. Moreover the aerodynamics of normal breathing, including a rather involved cycle of air velocities of inspiration and expiration, complicate the problem of determining what particle sizes will be picked up by the nostrils and whether the air-sampling device picks up the same range of particle sizes. The question of what portion of those particles entering the nostrils finally reaches the lungs is of less practical importance since all particles entering the nostrils and retained can be assumed either to be impinged on the mucous membrane from which they will be either absorbed or swallowed or to enter the trachea and possibly the lungs. In either case the rate and degree of absorption are apt to be considerably greater than the dermal route and beyond that the distinction is not apt to be of practical importance except possibly in the case of true vapors or gases where all the material can be assumed to reach the lungs.

Occupational Exposure

Estimating the exposure of occupationally exposed individuals is somewhat more satisfactory for two reasons; first, the concentrations encountered are apt to be greater and, therefore, more easily measured chemically; and secondly, the exposure is apt to be more specific—i.e., more limited in time and space—and, therefore, more easily defined. Thus, describing the exposure of a man spraying a given crop for eight hours a day with a particular model of sprayer is more satisfactory than describing the exposure of a tourist driving through an agricultural area where he may smell benzene hexachloride.

Nevertheless there has been surprisingly little effort made to measure directly the occupational exposure of agricultural workers if we are to judge from the literature. Batchelor and Walker (*1*) estimated the dermal and oral exposure to parathion encountered while spraying apples with air-blast equipment and with other older-style high-pressure hand equipment. This was accomplished dermally by fastening absorbent pads to various parts of the body during one or more complete spraying cycles. Chemical determination of the amount of parathion deposited per square inch of such pads during one timed spraying cycle permitted estimation of the amount that would contact a given area of exposed skin over a normal working day or while spraying a given number of acres. This estimate is dependent upon assumptions regarding the total area of exposed skin and the protection afforded by the clothing worn.

The respiratory exposure was estimated by a similar chemical analysis of the parathion absorbed on the filter pads of the respirator through which all inspired air had to pass. Laboratory tests had provided evidence that such pads were at least ninety per cent efficient in filtering out the parathion under the conditions of the test.

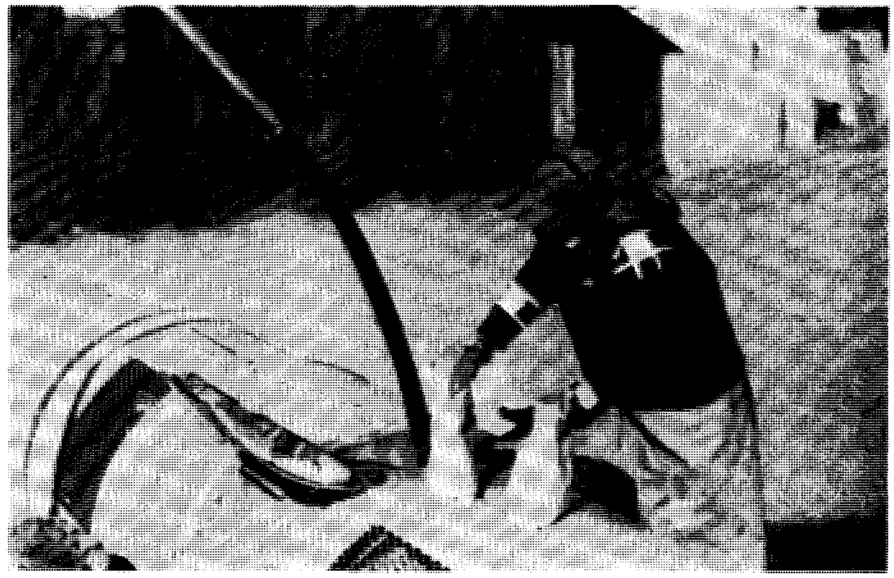
Culver *et al.* (*3*) used the same technique for estimating the exposure during the application of malathion or chlorthion by aerosoling equipment. They compared such estimates with similar ones based upon air sampling done at the same time and under the same conditions. These results indicate a discrepancy between the two methods by a factor of three to ten. They point out that the respirator pad technique involves a much reduced linear air velocity at the critical point (i.e. at the

Keeping dangerous insecticides under lock and key can prevent accidents

surface of the pads) as compared with the unimpeded nostrils because of the greater area involved. In spite of such complications the discrepancy between the two methods is not great when considered in the light of the much larger safety factor that must be involved in evaluating over-all health hazards.

Clinical Investigations Important

Following the detailed clinical course of actual cases of spray poisoning in man is of major importance in arriving at an evaluation of health hazards. The recognition of miosis or "pin-point pupils" as warning symptoms of TEPP exposure by crop-dusting pilots raised the serious question as to whether or not such miosis was accompanied by visual disturbances which might be a hazard to the pilot who is dependent upon good eyesight for safe flying of his plane. Information on the pattern of cholinesterase depletion and recovery with exposure to different cholinesterase inhibitors has helped to evaluate such problems as how soon a patient can return to work and it has permittted routine cholinesterase determinations among occupationally-exposed individuals to warn of unsafe practices. Careful investigation of reports of pesticide intoxication has permitted the weeding out of misdiagnosed cases and thus reduced groundless fears and at the same time it has permitted pin-pointing the situations that actually result in poisoning cases with the greatest frequency. It is surprising how often this type of investigation requires real "detective" work. Frequently otherwise well-informed sources of information will attribute the illness to one pesticide or situation when careful investigation proves a different cause. In one unpublished case several workmen were reported poisoned by an insecticide and the symptoms and circumstances seemed to fit reasonably well except for one patient who reported insufficient exposure. Careful investigation identified the complaints as a gastroenteritis and absolved the insecticide.



Dermal exposure of a spray man can be estimated by determining chemically the amount of deposit on absorbent pads placed at various positions on his body

One of the serious clinical problems yet to be solved is the importance of pesticides as allergens. Air-sampling and surveys of the type previously described may rule out systemic poisoning among residents with only environmental exposure, but the nature of allergic reactions is such that some individuals may react to concentrations too low to measure chemically. The entire technique of identifying allergens is difficult, complicated by false positive reactions and multiple sensitivities. Nevertheless in an over-all evaluation of health hazards it is important to have some objective estimate of the frequency with which allergic reactions occur among people with different types of exposures.

Whereas it is obvious that the final evaluation of health hazards must be carried out with humans under conditions of actual use, it is equally obvious that the general population must be exposed to unmeasured risk while such evaluation is taking place. To reduce this element of temporary uncertainty to a minimum it is most desirable to study humans exposed under controlled conditions. This type of controlled exposure study must be done with volunteers under rigid safeguards. Much has been written about the legal and ethical aspects of such experimentation on human subjects. [See for example the symposium in *Science*, **117,** 205 ff. (Feb. 27, 1953)]. Such studies may involve closely observed exposures under conditions already approved for the general population as when a group of volunteers ate fruit treated with demeton according to approved recommendations (*12*) or it may involve exposures to

Table of various LD_{50} values for DDT. Such information needs to be interpreted before estimating health hazard

Range of LD_{50} Values Determined by Different Authors for DDT for Several Routes of Administration and Several Species of Animals

(Values in milligrams of DDT per kilogram of body weight)

		Species					
Route	Formulation	Rat	Guinea Pig	Rabbit	Cat	Dog	Monkey
Intravenous	Homogenate	47	...	30–41	32	68	55
Oral	Solution	100–280[a]	400–560	228–1770	200–410	300	...
	Undissolved	500–2,500	2,000	275	...	...	...
Dermal	Solution	250–3,000	1,000–2,500	...	...	...	...
	Undissolved	1,000,000	2,500–2,000,000	250,000–500,000	...	...	...

[a] These figures involve solutions in various digestible oils. A value of 800 mgm./kgm. has been given for a solution in mineral oil which is both undigestible and laxative.

Source: *Hayes, Wayland J., Proc. 39th Mid-year Meeting Chem. Spec. Mfgrs. Assoc.*

relatively unknown hazards such as the scientists and others who first exposed themselves to DDT in order to expedite its use in the treatment of humans for typhus control. Such experiments, if properly conducted, go far toward a final evaluation of health hazards while restricting exposure to a small group who willingly undergo whatever dangers may be involved while in a favorable situation both as regards prompt medical attention if ill effects are encountered and also where maximum good can result from the observations.

An adequate evaluation of health hazards from the agricultural use of an insecticide can thus be said to require first that the basic pharmacodynamics of the pesticide in question be elucidated including rate and degree of absorption by various routes, mode of action, toxic levels, and antidotes or other methods of treatment, and secondly that a careful study be made of the conditions of use and the measurement of potential exposure by various routes under those conditions. From a practical standpoint this is followed by careful clinical investigations of poisoned individuals, preferably human volunteers who have been exposed under controlled conditions. Before the material attains widespread use it would be wise to evaluate the effectiveness of available protective devices. And finally, the evaluation should be rounded out by a continuing survey of actual effects, if any, on the exposed population. This final step can be reduced almost to the vanishing point slowly or rapidly as the results show the hazard to be great or small but it should never be lost sight of completely as long as the pesticide finds continuing use.

Literature Cited

(1) Batchelor, G. S., and Walker, K. C., *Arch. Ind. Hyg. and Occupational Med.*, **10**, 522–9 (1954).

(2) Bradley, W. R., J. Agr. Food Chem., **2**, 455–6 (1954).

(3) Culver, D., Caplan, Paul, and Batchelor, G. S., *Arch. Ind. Health* , 1955, in press.

(4) *Federal Register*, **20**, 1473–1508, Finding of Fact No. 22 (March 11, 1955).

(5) Fowler, Richard E. L., J. Agr. Food Chem., **1**, 469–73 (1953).

(6) Hayes, W. J., Jr., and Pearce, G. W., J. Agr. Food Chem., **1**, 466–9 (1953).

(7) Hazelton, L. W., J. Agr. Food Chem., **2**, 452–4 (1954).

(8) Neal, Paul H., Dreessen, W. C., Edwards, T. I., Reinhart, W. H., Webster, S. H., Castberg, H. T., and Fairhall, L. T., Public Health Bull. **267** (1941).

(9) Seevers, M. H., *J. Am. Med. Assoc.* **153**, 1329–33 (Dec. 12, 1953).

(10) Sumerford, W. T., Hayes, W. J., Jr., Johnston, J. M., Walker, K. C., and Spillane, J., *Arch. Ind. Hyg. and Occupational Med.*, **7**, 383–98 (1953).

(11) Technical Development Laboratories, CDC, Public Health Service, U. S. Dept. of Health, Education and Welfare (unpublished data).

(12) Upholt, W. M., Quinby, G. E., and Batchelor, G. S., Proc. Wash. State Hort. Assoc. 1954, pp. 217–20 (1955).

(13) Walker, K. C., Goette, Mary B., and Batchelor, G. S., J. Agr. Food Chem., **2**, 1034–7 (1954).

Hat, respirator, natural rubber gloves, long sleeves, boots are among items in well-dressed sprayer's attire

Case III

The importance of careful clinical study of all actual cases of poisoning is shown by a case reported by E. M. Dixon ("Dilatation of Pupils in Parathion Poisoning"—unpublished manuscript). Constriction of pupils or miosis is a condition commonly associated with poisoning by organic phosphorus insecticides. In fact this condition is so well known that it seems to be a reasonable diagnostic sign for physicians. However, V. N., a 15-year-old male had been engaged in loading a 45% solution of parathion into airplanes and in flagging for the pilot. After two weeks of irregular exposure, on July 11, 1953, he spilled a small amount of the solution on his skin. Within an hour he developed nausea, vomiting, headache, diaphoresis, confusion, and awkward gait. However, when first seen by the physician the patient's pupils were dilated. In view of the extreme heat of the day and the dilatation of the pupils, the physician felt that the patient was suffering from heat exhaustion, though he administered atropine sulfate. There seems little doubt that this report will aid physicians in the future to make more prompt differential diagnoses. Proper treatment can therefore be speeded, and in turn reduce the ultimate health hazard involved.

Case IV

The occurrence of readily recognizable warning signs or symptoms such as pin-point pupils in pilots from exposure to TEPP may reduce significantly the hazard of a given material. On the other hand Bidstrup and Payne [*Brit. Med. J.* (4722), 17–19, July 7, 1951] have described several deaths from dinitro-*o*-cresol in which the only symptoms were not easily recognized and were rapidly followed by death. One of their cases had applied DNOC as a weed-killer for less than a month. Although his wife had noticed that he was unwell and had been perspiring excessively for a few days before his death, the man himself did not complain of symptoms until shortly before his admission to the hospital, where he died. He had completed a full day's work on the day of his death.

On the day before the death of another of their cases the deceased's landlady had observed that he was perspiring freely and was unusually thirsty. In spite of these symptoms, he went to work and returned at 8:00 P.M. ill. At 8:30 P.M. he was much worse and died in the hospital a short time later.

Regarding the third of their cases, it was reported that he was sweating profusely and his skin was stained yellow but there was little to suggest at this time that he was seriously poisoned. The doctor recommended his admission to the hospital only because his co-worker had died. Yet he died in coma less than three hours after he was first seen by a doctor.