Bull. Org. mond. Santé)
Bull. Wld Hlth Org.) 1959, 20, 891-912

THE TOXICITY OF DIELDRIN TO MAN
Report on a Survey

WAYLAND J. HAYES, jr, M.D., Ph.D.

Chief, Toxicology Section,
Communicable Disease Center, Public Health Service,
US Department of Health, Education, and Welfare, Savannah, Ga., USA

SYNOPSIS

Increased use of dieldrin for malaria control has been caused by several factors, including sporadic resistance of some vectors to DDT. Poisoning of spray-men by dieldrin has been recognized in five widely separated countries and reported informally from several others. In some cases illness has recurred months after the last exposure. Observations of antimalaria programmes in Kenya, Tanganyika, Indonesia, India (Bombay State), and Iran and a review of the relevant literature have shown that the hazard associated with dieldrin is proportional to the degree of workers' exposure as determined by concentration of spray, area of bare skin, duration of contact, and lack of hygiene. Measurements of workers' exposure and a review of toxicity by different routes incriminates skin contamination as the greatest hazard under practical conditions. It is considered that dieldrin should not be used without justification ; if it is required, then certain individual and group protective measures listed in this paper may minimize, but not necessarily eliminate, the risk. The author enumerates certain features of the toxicology of dieldrin which require intensive research.

There has been an increase in the number of countries from which reports have been received of poisoning of workers carrying out indoor residual spraying with dieldrin in antimalaria programmes. There has also been an increase in the number of species of *Anopheles* showing resistance to DDT. In many instances, dieldrin has been the most effective insecticide available to control these resistant mosquitos. For this and other less cogent reasons, the use of dieldrin has increased in countries where workers are not accustomed to the use of toxic chemicals. The World Health Organization is actively supporting antimalaria programmes in several of these countries.

Because of these facts and because the dosage of dieldrin which spray-men receive is so intimately connected with the spraying practices which they employ, the World Health Organization sent the present author as toxicologist to observe actual programmes in Kenya, Tanganyika, Indonesia, India (Bombay State), and Iran. This report presents the observations

and conclusions arising from the survey and from a review of the relevant literature.

The clinical character of dieldrin poisoning in man is well known (Blazquez & Bianchini, 1956, 1957; Hayes, 1957; Patel & Rao, 1958; see also Haworth [1]) and is touched on only incidentally in this report.

Observations

Nandi Project, Kenya

This project was carried on using dieldrin for three years (1954-56) and discontinued because malaria control was considered adequate and it was desired to follow the epidemiology without further use of insecticides. The occurrence of malaria had been epidemic. The parasite rate had risen to about 60% every 2-3 years among a population of about 80 000 people; it was supposed that each epidemic spread from hyperendemic areas on two sides of the Nandi region. However, the epidemics were never fully explained. *Anopheles gambiae* was presumably the main vector; its incidence was low during outbreaks but may have been high during the time of actual transmission. It was not fully ascertained whether biting was mainly indoor or outdoor. In any event, *A. gambiae* virtually disappeared from huts and the parasite rate fell to near zero while dieldrin was used.

The conditions under which dieldrin was used safely in the Nandi project are briefly as follows. About 40 labourers and 15 supervisory staff were employed each year for a maximum of four months in the application of 1.7% dieldrin. New workers were employed each year. The men were in the habit of washing frequently and they continued this practice when they were at work without the necessity of being constantly reminded. Soap was supplied free. In addition, a rather impressive array of protective equipment was supplied and was actually used. It is noteworthy that face shields were well accepted. Although uniforms were not supplied, the workers generally wore old clothes during spraying and changed to fresh clothing after bathing at the end of the day. It is said that a pump pressure of 50-70 pounds per square inch (p.s.i.) (or about 3.5-5 kg per cm^2) was used.

Two instances of undiagnosed chest trouble and two cases of dermatitis were noted during the first year of spraying. The possibility that these illnesses were related to dieldrin was considered, and although it could not be ruled out completely, it seems very unlikely because similar difficulties have not been prominent in other programmes that have involved serious poisoning.

One man died after ingesting an unmeasured quantity of dieldrin which he had stolen while he was employed on the Nandi project.

[1] Haworth, J. (1955) *Observations on possible toxic effects of dieldrin on mammals* (Unpublished working document WHO/Insecticides/60)

The project did result in the death of a few cows and goats. It is thought that the animals drank dieldrin or licked up spray which had been spilled. In at least one instance the spray-men ate a goat which had just died of dieldrin poisoning; they suffered no observable effect.

Although they are not directly related to the question of the safety of dieldrin, certain other observations are of interest. A few months after the first spraying, there was a great increase in houseflies. The local people generally attributed this increase to the use of dieldrin but there is some question whether a relaxation of sanitation may not have been to blame. In any event, it is certainly a fact that lizards and some other predators of flies were killed. Dieldrin was not applied to breeding sites and it seems, therefore, that it cannot have affected the immature stages of the flies which, in fact, were observed to be unharmed. The same degree of increase in flies is said to have followed the use of lindane. The resistance of houseflies in Kenya to insecticides has been reported by McMahon (1957).

In addition to the Nandi project and Taveta-Pare project (see below), it is known that Mombasa has been partially protected from malaria by the spraying of huts in a 2-mile barrier zone around the city. The insecticide is sprayed on a short time before the rainy season and takes only a few weeks to apply.

Taveta-Pare Project, Kenya and Tanganyika

The Taveta-Pare project was established in June 1955 entirely for experimental purposes. The primary objective was a study of the general health of a population associated with the control of endemic malaria. Secondary objectives included studies of the persistence, effectiveness, and safety of dieldrin. The population among whom malaria has been controlled have been subjected to a general physical examination and their weights and haemoglobin and serum protein levels recorded. Similar examinations have been done on the spray-men at the beginning and end of each spraying cycle. The dieldrin deposits have been investigated and the application procedures regulated to produce a theoretical deposit of 0.4-0.5 g per m^2 and a measurable deposit of 0.3-0.4 g per m^2. A very detailed study of the exposure of the workers has recently been published by Fletcher et al. (1959).

Much additional information about the conditions under which dieldrin was used safely in the Taveta-Pare project has also been given by the same authors. In summary, the use of a dilute formulation (0.55%) of dieldrin and the use of acceptable, effective devices has limited the exposure of spray-men to a measured skin dose of 1.8 mg per kg of body-weight per day. This exposure is undoubtedly reduced in practice by washing with soap and water. However, it has not been possible to measure the degree of reduction. The pump pressure was 50 p.s.i. (3.5 kg per cm^2).

For the purpose of evaluating safety, the project offers the advantage that most of the men with significant exposure have been employed throughout the duration of the project, that is, for a total of four years or about 900 days of actual spraying. The only difficulty in this evaluation is that the total number of such men is small, being only 10, of whom only 8 have participated in the entire project. Statistically, it is possible that no poisoning would occur in such a small sample under conditions which would produce poisoning in as much as 10% of a large population at risk. However, the fact remains that no instance of poisoning has been revealed either through examination or through the complaints of the men. It seems likely that good morale is important in obtaining the full co-operation of spray-men in safety measures. Spray-men on the Taveta-Pare project are well paid relative to other local labour.

By direct observation, I was able to confirm that some contamination of the workers does occur, but that it is minimal. The conditions of spraying are frequently difficult: I saw a man spray an outbuilding which was so small that he had to kneel during the entire operation. At the end of the day's work the spray-men's hats and face shields were grossly wet with spray. The surfaces of the right shoulder and sleeve of the spray-men's overalls were slightly damp but the dampness did not extend through the cloth.

On one occasion a pumper was seen to pick up the small knapsack in which dieldrin powder is carried in such a way that part of his hand was coated with the powder. In another instance, soil wet from spillage was left uncovered and accessible to chickens.

Although most houses were completely cleared of furnishings, bags of rice or cereals (probably weighing about 70 kg) were sometimes left in houses during spraying because they were too heavy to move. Samples of maize and maize flour from such bags left in houses during spraying have been examined and the dieldrin content has been found to range from 0 to 2.8 parts per million.

In the Taveta-Pare area, spraying is done with stirrup pumps rather than with compression sprayers, and these pumps are thought to have the advantage of being carried in such a way that the left shoulder and back are not contaminated. I observed some contamination of the side of the right leg of men carrying stirrup pumps and related equipment; however, the contamination was not wet but dusty and, therefore, not so likely to reach the skin as the leakage from a compression sprayer.

Some chickens have been killed by dieldrin during the project. Many more were killed during the first cycle of spraying than during subsequent cycles. This is attributed to the fact that flies were not resistant to dieldrin during the first cycle so that many flies were killed and then eaten by chickens at that time.

The following facts, although not directly related to the Taveta-Pare project, are of interest. In 1956, 2% granular dieldrin was used for the control

of mosquito larvae in tests at Arusha, Tanganyika; the men used gloves and masks and washed; there were no untoward effects.

Dieldrin has also been used to a very small extent at the same station for crop spraying. Dieldrin emulsion was mixed in the spray tank of the aircraft so that exposure of the applicators was minimal. Dieldrin has also been used in Uganda as a residual spray against tsetse flies. An emulsion was applied to vegetation, especially the underside of tree limbs. The work was closely supervised and resulted in no known injury.

In Kenya, dieldrin is used for locust control about four months each year (personal communication from Dr Stott, Special Medical Officer, Department of Labour, Kenya Government). Application is made by ground teams and also by aircraft using a low-volume exhaust sprayer. The formulation used is a 20% solution in kerosene. Very little of this kind of application has been made, but it is proposed to expand the work.

Indonesia

Malaria control in Indonesia is carried out by the Government of Indonesia through the Malaria Institute (Lembaga Malaria) with the technical and financial aid of the World Health Organization and the International Cooperation Administration. Representatives of the three agencies form a board which sets policy. However, execution of the work and the collection of epidemiological and entomological statistics are the responsibility of the Malaria Institute. Very important in the long chain of command are the regency doctors, who carry on private practice as well as official duties.

The project is aimed at malaria control in Java. Houses in some parts of the island have not yet been sprayed. The resistance of the chief vector (*A. sundaicus*) in some parts of the coastal area led to the substitution there of dieldrin for DDT in 1955. The substitution of dieldrin was extended to many areas beginning in 1956. The insecticide was used at a rate of 0.25 g per m^2 at first, but later at 0.50 g per m^2. Dieldrin has been used in the three provinces of Java. The substitution was not confined to areas where resistance had been demonstrated.

The number of workers who have been exposed to dieldrin is great and the amount of dieldrin issued is also great, as shown by the following figures for Central Java alone up to January 1958:

Residency	*Cases of dieldrin poisoning*	*Dieldrin issued (kg)*
Semarang	23	33 702
Pati	15	15 225
Pekalongan	1	36 055
Kedu	4	9 526
Banjumas	0	12 841
Total	43	107 349

Because of the size of the project and for other reasons it was not possible to collect information on spraying conditions in the same detail as was possible for the Taveta-Pare project, for example. Briefly, the teams which I observed using dieldrin were no more careful than the team which I saw using DDT. On one occasion, I saw a mixer scooping up dieldrin powder with his bare hands so that his hands and wrists became completely white. He rinsed the material off with water but without removing his wrist-watch. Frequent contamination of the hands with a dilute suspension was the rule rather than the exception. It was my impression that a smaller volume of spray mist bounced back on the Indonesian spray-men than on the spray-men in the Taveta-Pare area. This seems to be explained by the fact that the average Indonesian house is larger than the African hut and is frequently well ventilated either by a completely open space between the wall and the roof, or by many small holes in the matting which forms the walls, or by both. On the other hand, the Indonesian spray-men had very much more skin area exposed to spray than their African counterparts. Other differences are the greater concentration of the spray used in Indonesia and the lack of any vacation period for the Indonesian workers. The pump pressure measured in Indonesia was variable and often high.

Little or nothing is removed from Indonesian houses before they are sprayed. Matting for beds is rolled up. Some food is covered and some vessels for food are overturned so that the spray falls on the underside. However, even these precautions are not invariably taken; and a case has been reported in which the spraying of cooking utensils was followed by poisoning. Only the mother in the family ate the contaminated food and only she became sick. The character of the disease is not known but it is understood that the patient survived.

The occurrence of the 43 cases of dieldrin poisoning in Central Java mentioned earlier became generally known as the result of observations by Dr R. Hasmo Soegijarto, Malaria Advisor to the Inspector of Health for Central Java. He described 15 of the cases in some detail (personal communication, 1958). The reported signs and symptoms included headache, sweating, weakness, loss of consciousness, and convulsions. He regarded the diagnosis as tentative, largely, it seems, because many of the fits occurred when the workers were going to and from home rather than when they were in direct contact with dieldrin.

The histories of nine of these cases, whom I was able to examine myself, are given below. The case numbers correspond to those assigned by Dr Soegijarto with the exception of cases 16 and 17, on which he did not report.

Case 1. L., a 20-year-old unmarried spray-man, worked with DDT for one year and with dieldrin for one year before being affected. He wore a sports shirt with long trousers while spraying. He had no hat or shoes. He washed only his hands while at work and used no soap because none was provided. He bathed at home with his own soap but it

took him about two hours to go home after work and he bathed only after eating and resting. He was aware that spray fell on him while he worked. He worked 25-26 days per month, including half a day on Friday. He had Sundays off.

In August 1957 he was hospitalized for 15 days for typhoid fever and he rested for a month after leaving the hospital. Shortly after returning to dieldrin spraying he suffered a fit. At that time he complained of weakness, headache lasting about an hour, and nausea, which was present before as well as after the fit. He was unconscious for about half an hour. The relationship of the first and subsequent fits to dieldrin exposure was as follows:

11 September 1957 22 September 1957 4 January 1958 4 February 1958	Continued dieldrin exposure
1 June 1958	Office work during March and April and DDT spraying during May and June

The last fit, which lasted about five minutes, was observed by the spray-man's brother, who was a supervisor of the squad. There was no personal or family history of convulsions. The man stated that he felt well and that he had grown bigger and stronger while working as a spray-man. No neurological abnormality was found on examination.

Case 3. J., a 21-year-old married spray-man, began working with dieldrin in April 1956 having had no previous contact with insecticides. He wore shorts and a vest. He had no shoes and no hat. No soap was supplied to the unit. He was aware of dieldrin on all parts of his body and claims to have bathed with soap at home before eating his evening meal. He had 9 attacks, characterized by convulsions and unconsciousness lasting about a minute. The fits occurred as follows: August or September 1957, 1; October, 1; December, 4; January 1958, 3. He continued to work with dieldrin during this entire period and it was not until March 1958 that he was transferred to DDT spraying. At least some of the 9 attacks were treated in a polyclinic with a diagnosis of malaria. There was no history of previous fits in the man or in his family. On 3 July 1958 he stated that he felt well. The neurological examination was normal.

Case 6. A., a 20-year-old spray-man, began working with dieldrin in March 1957. His clothing and bathing habits were similar to those of other spray-men. According to a diagram prepared by him and his supervisor, he had one fit in July, four in August, and three in September 1957. He worked with DDT during February, March and April 1958 and did office work during May and June. During June he had five fits, making a total of 13. Thus, these last convulsions were a little over four months after his last exposure to dieldrin.

Case 8. S., a 20-year-old spray-man, worked with DDT from July 1955 through March 1956 and with dieldrin from April 1956 until March 1958. He wore long trousers and a vest but no hat or shoes. Soap was not supplied at work. He washed without soap before eating at home and bathed with soap in the evening. His first attack was in December 1957. It was characterized by temporal headaches, momentary unconsciousness without falling and a sense of suffocation which did not interfere with work but which required deep breaths. There were several similar attacks. He denied that he or anyone in his family had had this trouble or frank convulsions. (The illness of this man appears to have been entirely subjective. It seems impossible to determine at this time whether he suffered from autosuggestion or from something analogous to *petit mal* epilepsy.) The neurological examination was normal.

Case 9. S., a 25-year-old married spray-man, began using DDT in September 1954 and changed to dieldrin in June 1956. He wore a sports shirt, shorts or long trousers,

and a cap with a visor. He had no shoes. His history of bathing was similar to that of the others. He occasionally bathed in the fields where there was plenty of water available. He had a total of four fits, which occurred in June, July and October 1957 and February 1958. The first two fits were observed by his wife. The fits were accompanied by headache and nausea. After each attack, he was treated in a hospital out-patient department but the composition of the pills given is not known. In February 1958 the man was transferred to DDT spraying, after which he had no further attacks. There was no personal or family history of fits. The neurological examination was normal.

Case 12. B., a 20-year-old spray-man, sprayed DDT from November 1955 through March 1956 and sprayed dieldrin from April 1956 until March 1958. He wore long-sleeved shirts and long trousers but no hat or shoes. He washed his hands without soap when he finished work and bathed with soap in the evening after eating. In February 1957 he had headache, nausea, and vomiting but no loss of consciousness. The headache had a bilateral temporal distribution. He had had headache before but not one of such long duration. He received treatment from several polyclinics but it was not effective in relieving the headache or other symptoms. The neurological examination was normal.

Case 15. K., a 20-year-old spray-man, worked with dieldrin for 10 months before becoming ill in October 1957. His clothing and bathing habits were similar to those of his fellows. His supervisor saw him have a fit, which lasted five minutes and came without apparent warning. While the patient was cycling to the hospital one hour later, he fell and had another fit. It was followed by headache, weakness and nausea. He rested for two months after leaving the hospital and then began work with DDT. There was no personal or family history of epilepsy.

Case 16. S. was dismissed from work when he had his first fit in August 1957. He had worked with dieldrin since March 1957. He had two more fits during the week following his dismissal. He was then treated by a doctor. Later he returned to his home village. He is now well. There was no history of epilepsy in the spray-man or his family.

Case 17. K. began spraying dieldrin in April 1956 and continued until April 1958, when he transferred to DDT spraying. He wore shorts and a vest. He had a cap with a visor but no shoes. No soap was available at work. After going home on his bicycle he washed his hands with soap before eating. Later he bathed with soap. He had three attacks, all of which were on a single day in November 1957. He fell from his bicycle on the way to work and hurt his leg. He was momentarily unconscious and woke with headache and nausea but no vomiting. While at work he had another attack which was seen by the owner of a house. He was sent home by his supervisor. Having reached home, he fell again while on his way to the river to defaecate. It was reported that he had no convulsion during his brief periods of unconsciousness. Neurological examination, done on 3 July 1958, was normal.

* * *

Six of the above cases (Nos. 1, 3, 8, 9, 12, 17) were from the Kendal area, where 13 men were said to be sick out of 15 squads (15 supervisors, 15 mixers, 75 spray-men).

It is noteworthy that the Regency Supervisor stated to me that he had never seen anyone have a fit except the men listed as cases 15 and 16. He was in charge of 50 spray-men (10 squads), among whom three (including cases 15 and 16) had been poisoned.

During the period when cases of poisoning were reported from Central Java only, there were many speculations to explain the supposed distribution. It was alleged that the spray-men in Central Java were more careless, that supervision was poor in some areas, that there had been a drought so that it was impossible for the men to bathe or obtain adequate food

during the period when illnesses occurred and, finally, that illnesses had occurred in different areas in direct proportion to the amount of dieldrin used. Although it was not possible to investigate each of these explanations fully, I encountered no evidence that any of them was valid. There was little difference in the care which I saw used in spraying in West and Central Java. There is no significant relationship between the reported occurrence of poisoning and the amount of dieldrin used (see the tabulation on page 895).

The true difference lay in reporting rather than in other factors. The physicians who had observed cases of dieldrin poisoning in West Java and in East Java had not yet reported their findings to the leaders in Djakarta.

The Residency Physician for West Java stated that he had treated mixers and spray-men from several squads who had suffered sudden falls and convulsions. The fits lasted 5 to 10 minutes. They involved foaming at the mouth and rolling up of the eyes. Fits were usually followed by giddiness, headache, and vomiting. The patients were treated by giving them, while they were still unconscious, the juice of a sour fruit which is commonly available in Indonesian kitchens. The affected workers were given a two-week rest period and then returned to dieldrin spraying. At least one man had a second fit about a month after returning to work. The initial attacks followed 6-8 months of exposure to dieldrin, except in one instance in which a connexion between the man's smoking habits and the early onset of sickness was suspected. The first recognized case occurred in December 1956, 6 months after spraying with dieldrin was begun in June. Similar illness was unknown in the area before dieldrin was used.

The Residency Physician estimated that 14 of the 35 spray-men in his immediate area had been made sick by dieldrin. Reports of similar illness had come to him from other parts of the Residency and he considered poisoning by dieldrin to be a great problem in West Java, even though no human deaths had occurred.

In East Java, 15 cases of dieldrin poisoning were observed by the Deputy Inspector of Health, Dr M. Imanoedin (personal communication, 1958) among 833 labourers of all categories up to September 1958. One case appeared after 6 months; two after 7 months; two after 8 months; one after 9 months; three after 10 months; two after 11 months; one after 12 months; two after 14 months; and one after 15 months. Illness was characterized by headache, blurred vision, insomnia, general malaise, sudden falls, and, in all instances, convulsions with loss of consciousness. Examination of blood, urine, and faeces in all the patients and complete neurological examination of three of them failed to reveal any abnormality.

As with cases of poisoning in man, the poisoning of domestic animals was reported first in Central Java and it received more attention there than in other areas. However, it seems probable that there has been no major difference in the incidence of animal deaths in the three Provinces. Cats and mice are reported to have died following the use of dieldrin in West

Java; and in Central Java so many cats were killed that the price of cats more than doubled. The early reports about the death of chickens and other animals in Central Java were probably exaggerated. However, C. A. Ferullo (personal communication, 1957) has shown by experiment that a 5% mortality is to be expected in chickens from villages sprayed with dieldrin, and when the recommended precautions are not applied a much higher mortality is to be reckoned with. No evidence has been advanced to prove that dieldrin has been responsible for the deaths of horses, buffaloes or goats.

India, Bombay State

The use of dieldrin for malaria eradication in Bombay State was undertaken for experimental and other purposes unrelated to any resistance of the local vector. The use of dieldrin as an adulticide for filariasis control is also considered by some to be experimental.

All the important matters concerned with the occurrence of poisoning by dieldrin in Bombay State have been published by Patel & Rao (1958) and will not be repeated here. However, a few points are discussed. Incidentally, 5 cases of poisoning have been reported from another part of India (Rahman et al., 1958).

On direct observation, it is evident that the spray-men in Bombay State have a relatively greater part of their bodies exposed than workers in most other parts of the world. This is largely necessary because of the hot, wet climate. However, this exposure of a large skin area may well have been an important factor in permitting the occurrence of poisoning in spite of relatively short cycles of spraying (32, 71 and 78 days respectively) and relatively long intervals between cycles (98, 63 and 31 days respectively). Spraying is timed according to the monsoons. No relationship between personal bathing habits and susceptibility to poisoning has been noted.

The use of dieldrin for malaria eradication was stopped from late November to 16 June 1958. During this period protective clothing was designed and made from the plastic liners of the drums in which dieldrin is shipped. The clothing consisted of caps with visors and coats of approximately knee length with three-quarter-length sleeves. The legs and feet of the workers were uncovered and the caps offered, at best, only partial protection to the face and neck. Protection of the lower part of the face was given by a surgical mask. The spray-men were equipped with "bent nozzles", i.e., spray wands bent at about a 45° angle about 7-10 cm below the attachment of the nozzle.

Inspection of 25 of these workers at Padgha near Thana at the end of a day revealed that in many instances their feet and legs were white with spray residue. Some of them had grossly visible deposits of wettable powder on their arms and hands beneath their gloves. Although the men

had been shifted to DDT some time earlier, experience indicates that in spite of the best efforts of supervision, their use of dieldrin may not have differed greatly from their use of DDT.

The same observations largely held true for spraying which was observed in another village (Manelau, at some distance from Poona). The spray-men were disciplined and efficient, but the fact that they were not completely covered brought them in direct contact with more spray mist than necessary. Furthermore, houses were not cleared before spraying. Cooking vessels and trays were sprayed freely. It was claimed that the food vessels were all washed. DDT was being used but with dieldrin a single contamination of food would be dangerous. During the spraying process, children wandered in and out and some of them got visible spray on their skin and hair. Some of the compression sprayers were equipped with constant pressure devices adjusted to 10 p.s.i. (0.7 kg per cm^2). They were considered entirely satisfactory. Most of the sprayers available were not equipped with such devices and were operated at pressures of 20-40 p.s.i. (1.4-2.8 kg per cm^2).

Since the published report by Patel & Rao (1958), there have been further developments which will be reported by those investigators. Briefly, a detailed laboratory and neurological examination has been made of four of the original ten patients from the malaria control team, and new cases have occurred following a temporary return of the workers to dieldrin spraying.

Neurological examination of four men, 3-4 months after their last exposure to dieldrin, showed completely normal findings. Only one of the men showed a dysrhythmic electro-encephalogram, while another had an epileptic fit that was observed by a nurse in the hospital. Various laboratory tests including liver function tests and examination of the cerebrospinal fluid were normal in the four men, but three of them showed an eosinophilia ranging from 8% to 34%, which is unusually high for the area. One of the patients gave a history of unconsciousness without jerking.

The occurrence of five new presumptive cases (one involving a fit) following the reinstatement of dieldrin on 16 June led to a return to DDT on 28 June.

Patel & Rao pointed out that dieldrin had been used in Bombay State for periods of 5 months or less in 1955 and 1956 without any reports of toxicity. They felt, however, that the possibility that poisoning did occur could not be completely ruled out.

These authors have published their hypothesis that dieldrin poisoning involves an allergic phenomenon. The matter is certainly worthy of consideration, but several facts need to be kept in mind in reaching a final decision. Of the 20 cases reported, five occurred in the first cycle during which the worker was exposed (14, 16, 26, 36 and 60 days respectively). Since the longest spray cycle reported was only 78 days and since it has frequently taken several months of exposure in other programmes to

produce dieldrin poisoning, it may require no special explanation that the other cases did not occur in the first spraying cycle during which the worker was exposed. Furthermore, the cases which occurred in a worker's second or third spraying cycle did not appear on first re-exposure, as one would expect in case of hypersensitivity, but only after several days or even weeks.

In case No. 4 reported by the same investigators, a fit followed exposure to BHC some 8 months after the last exposure to dieldrin. This relationship may have significance. However, there have been relapses in some patients who have been poisoned by dieldrin and who have had no further exposure to dieldrin or other insecticides. Thus the possibility must be considered that the fit in case No. 4 was in the nature of a relapse in a previously unrecognized case.

Iran

Dieldrin has been used for indoor spraying only in the southern portion of the country, where the malaria vector has developed resistance to DDT. The compound has been used for two cycles of 60 days or less, separated by an interval of 5 months. The most recent spray cycle was completed in April 1958. About 1740 spray-men and 174 mixers were exposed but only for these short periods. Their bodies were fully covered but their hands and faces were generally bare. They were given free soap, and they washed before eating and after work.

Spraying of DDT was in progress in the Teheran area in July 1958. The workers were well protected except that their faces, hands and ankles were bare. They were careless in handling the wettable powder and suspension with the result that their hands were frequently soiled either in mixing the suspension or in transferring it to the sprayers. During the spraying some vessels for food were contaminated and the mangers from which animals ate were sprayed thoroughly.

It was felt that the plastic veil would be acceptable to spray-men in Iran partly because of its similarity to the head-dress worn by Arabs.

Discussion

Dieldrin is a toxic substance which is freely absorbed by the skin. Dry dieldrin is absorbed about as easily as dieldrin put on the skin in solution. The insecticide is less than twice as poisonous by mouth as by skin application—an insignificant safety factor. Dieldrin differs very much from DDT in this respect. The oral toxicity of dieldrin is only 3-5 times greater than that of DDT. However, DDT is not readily absorbed by the skin even when in solution, and dry DDT is so little absorbed by the skin that toxicity is not evident.

The dermal toxicity of dieldrin has not been fully appreciated by some of those who have used the compound in antimalaria programmes. A relevant point which has been even more generally missed is that all of the unclothed skin of a spray-man (and, to a smaller extent, his protected skin also) is subject to constant contamination during the process of spraying. This " imperceptible " contamination is added to any visible soiling from spillage or other direct contact with dieldrin powder or suspension. Chemical measurements of " imperceptible " contamination during indoor spraying have emphasized the magnitude of the problem and also have shown the relative unimportance of respiratory exposure (Wolfe et al., 1959). These measurements are of special importance because it has commonly been assumed without any basis that the major source of dieldrin poisoning is respiratory exposure. This is an understandable mistake, because the great importance of gases, metal fumes, and silica dust in industrial medicine has led to great emphasis on respiratory exposure. It is also true that dieldrin is poisonous if it is inhaled. The crux of the matter is that only small particles can be inhaled, and nearly all the dieldrin in water-wettable powder is impregnated on particles too large to be inhaled. The spraying process does not grind the powder any finer. On the contrary, wetting the powder makes it more dense and spray droplets may be appreciably larger than the powder particles which they contain. It follows that measurement of the concentration of dieldrin in the air during spraying may be entirely misleading unless the particle size and the fact of dermal toxicity are taken into account.

If one assumes that man is as susceptible to dieldrin poisoning as are experimental animals, then the " imperceptible " mist of dieldrin suspension which falls on the unprotected face and lower arms of spray-men is sufficient to account for the incidence of poisoning which has been observed. This is not astonishing in view of the fact that during the working day the spray mist, which is imperceptible as it falls, often accumulates on the exposed skin to form an easily visible residue.

Another technical point is that any given dosage of dieldrin is absorbed more readily by a large area of skin than by a small area. This means that any increase in the area of skin exposed not only increases the dosage that will be received but facilitates absorption.

Poisoning of spray-men and mixers using dieldrin has been recognized in Venezuela, Ecuador, Nigeria, Java, and India. Informal reports indicate that it has occurred also in other places. Poisoning by dieldrin has not occurred in the Nandi or Taveta-Pare projects and has not been reported from Iran, Liberia, or the Philippines, where this insecticide is also in use.

The failure of poisoning to occur or to be reported in some places where dieldrin has been used is encouraging but—for very different reasons in different instances—must be viewed with scientific conservatism until further information is available.

Many of the cases which have been recognized as dieldrin poisoning have involved serious illness. The proportion of recognized cases showing one or more epileptic fits has varied from 47% to 100% in different countries. The occurrence of fits in a very high percentage of cases almost certainly means that some less severe cases were missed. In fact, there is no assurance that the complete spectrum of dieldrin poisoning is known at this time. Among the cases of dieldrin poisoning, there are at least six men who had one or more fits 15 to 120 days following the last exposure to dieldrin. It is probably too early to assume that some of these men will not have another fit. Furthermore, because it has not been possible to follow all cases of recognized poisoning even for a few months after dieldrin exposure had ceased, it is probable that the recurrence of symptoms was missed in some cases. Recurrent convulsions have been observed in experimental animals and occasionally persist until the animal dies at an old age. In addition to sudden falls, unconsciousness, and convulsions, another disturbing sign in some cases of dieldrin poisoning in man and animals is mental disorder. In man, the trouble has taken forms ranging from loss of memory, insomnia and nightmares to mania. It is reported that two men have died in convulsions following exposure to dieldrin. The cases have not yet been properly studied. It is therefore not possible to state whether either of them showed a syndrome clinically similar to that of poisoning observed in animals, which was characterized by complete loss of appetite and consequent severe weight loss and which was uniformly fatal in the absence of medication.

It is true that, after having a fit, some spray-men have continued their occupational exposure to dieldrin without disastrous effects. However, the recurrence of symptoms in men and animals after exposure has stopped raises the possibility that dieldrin produces a morphological and/or biochemical lesion which persists for some time and may give rise to recurrent illness. It may be assumed that, during exposure, dieldrin circulates in the blood and becomes stored in the fat. Unfortunately, practically nothing is known of the dynamics of dieldrin storage. It is therefore impossible to state the relationship between storage and the observed recurrence of characteristic illness following long intervals without re-exposure.

When poisoning by dieldrin has first been observed in a country, it has been a common practice to suppose that the victims were susceptible because of some inherent weakness. Infestation with worms, poor nutrition, " epileptic tendency " and inbreeding are some factors which have been suggested. Such factors are worthy of scientific consideration, but so far not a shred of evidence has been presented that they have any significance whatever in determining the occurrence of poisoning under practical conditions.

A vast difference has been observed between the spraying practices by which dieldrin is applied in different countries. Some of the main points

COMPARISON OF DIELDRIN SPRAYING PROGRAMMES IN DIFFERENT COUNTRIES

Country or area	Concentration of dieldrin and formulation	Area of spray-man's body which is bare [a]	Gross exposure	Duration of spraying		Interval between cycles (days)	Number of spray-men	Proportion of workers poisoned (%)	Proportion of cases involving fits (%)
				cycle (days)	total (days)				
Bombay State, India [b]	1.25 % suspension	Head, arms, lower legs	Mixed with hands	78	140	31	192	7	80
Bombay State, India [c]	2.50 % suspension	Head, arms, lower legs	Mixed with hands	32-71	160	63-98	105	10	100
							92	9	50
Ecuador	2.50 %								
Indonesia	1.25 % emulsion	Head, hands, lower legs	Frequent soiling of hands observed	365	852	0	145 [d] 35 [e] 833 [f]	11 [d] 40 [e] 2 [f]	88 [d] 100 [e] 100 [f]
Iran	1.25 % suspension	Face, hands	Disclaimed	45 [g]	90	150	670	0	—
Nandi, Kenya	1.7 % suspension	Hands, knee area (shorts and boots worn)	Minimal	90 [h]	270 [h]	275	90	0	—
Nigeria	0.68 % suspension and emulsion; 1.37 % suspension	Face	Frequent	77-98	341	77-99	40	10	100
Taveta-Pare	0.55 % suspension	None	Minimal	151-174	810	68-108	10	0	—
Venezuela	1.25 % suspension; 2.50 % emulsion	Face	Frequent soiling of hands in some groups	365	1460	0	285	18 [i]	47

[a] It is realized that parts of the body which are covered by some kind of clothing may really be exposed to dieldrin. This is especially important in the case of improperly used gloves.

[b] Antimalaria programme

[c] Antifiliariasis programme

[d] Central Java (values based on selected groups for lack of statistics for whole work force)

[e] West Java (values based on selected groups for lack of statistics for whole work force)

[f] East Java

[g] Maximum 60 days

[h] Maximum of 90 days for each worker

[i] For those working eight months or more, 26 %; for one sub-group, 50 %.

of difference are outlined in the accompanying table. Unfortunately, some of the values in the table are tentative. Furthermore, there can be no assurance that all of the important factors related to the safe use of dieldrin are now recognized. In spite of these handicaps, there is clear evidence of a direct relationship between dosage and the occurrence of poisoning. This is manifest in at least four ways:

1. The greater the concentration of dieldrin suspension used for spraying, the greater is the chance that poisoning will occur following a given period of exposure (see the table).

2. Under otherwise similar conditions, the greater the area of bare skin exposed during spraying, the more likely is poisoning to occur (see the table).

3. The longer the exposure (at least up to 2 years) under conditions which lead to some poisoning, the greater will be the total incidence of poisoning (Hayes, 1957). It seems certain that intervals between cycles of exposure allow some excretion of stored dieldrin, but the rate of such excretion is unknown. Rest periods may also permit some degree of recovery from other possible effects of dieldrin. The fact remains that the practical importance of rest periods in preventing dieldrin poisoning is not known.

4. Immediate washing of the contaminated skin is partially protective; delayed bathing offers distinctly less protection (Hayes et al., 1951). Although one may assume on logical grounds that the absorption of dieldrin continues as long as the compound is in contact with the skin, there is no objective evidence that washing which is delayed for several hours or more after exposure has any protective effect whatever.

Because of differences in one or more of the dosage factors just listed, the exposure of spray-men in those programmes under study which have not given rise to reported poisoning is recognizably less than that in those programmes in which poisoning has occurred. There is no evidence which would lead one to predict the occurrence of poisoning in those programmes in which it has not already occurred, provided the conditions of exposure remain unchanged. On the other hand, there are several reasons why it is impossible to guarantee that poisoning will not appear later even under the same conditions.

It is a general principle of toxicology that even the most poisonous compound may be used if adequate safeguards are provided. It does not follow that adequate safeguards can be provided under all conditions. One must face the logical possibility that some programmes, for reasons of climate, or finance, or the availability of competent supervisors, cannot provide the training, supervision and protective equipment necessary to reduce the incidence of poisoning among spray-men to a minimum. It is

worth mentioning, however, that the preconceived ideas of programme leaders have sometimes been important in causing the rejection of good equipment, which had proved acceptable under similar conditions in other places.

Recommendations

It is clear from the record of use that dieldrin is a dangerous compound. It should not be used for indoor spraying unless resistance of the vector to safer insecticides, or some other good reason, makes dieldrin really necessary for disease control. If those responsible for vector-control programmes consider it necessary to use dieldrin, then they have a responsibility to recognize the calculated risk. The present survey justifies the belief that the risk may be minimized, but not necessarily eliminated, by certain protective measures. These measures are consistent in principle with those previously recommended by the World Health Organization (1956) but are arranged here in approximate order of increasing expense. It appears that some programmes have not used all the facilities at their disposal to ensure the safety of their spray-men.

Suggested protective measures are as follows:

(1) Each worker should be told when he is hired that he is to work with a dangerous compound which has produced serious sickness in men like himself. Dieldrin poisoning and the protective measures which will be required should be described.

(2) Rigid supervision should be maintained to ensure the practice of:

(*a*) washing the hands at frequent intervals even though no contamination is visible;

(*b*) washing the hands and face with soap and water before meals and before smoking;

(*c*) washing with soap and water after each recognized contamination of the skin;

(*d*) bathing the entire body with soap and water at the earliest practical moment after work is finished for the day. It is sometimes stated that there is inadequate water for washing; to the toxicologist, there is always enough water for washing if there is enough for spraying. The cost of hauling the water simply must be counted in the cost of spraying.

(3) Free soap should be available for the washing recommended under items 2 and 4. It was found on one programme that a ration of 250 g of soap per man per week was adequate. In another programme, new soap was issued to each man when he exhausted his previous supply.

(4) Work clothing should be washed daily with soap and water. If this daily laundry is not done by an outside contractor, then it becomes a responsibility of each spray-man and must, of course, be done during working hours and under the supervision of a foreman, like any other duty for which the spray-man is employed.

(5) Arrangements should be made for each spray-man (including pumpers and mixers) to have at least two sets of work clothes with a high neck-line, long sleeves and long trousers. The work clothes are not to be worn after working hours. The clothing must not be worn with the sleeves or trousers rolled or with the collar open.

(6) Arrangements should be made to ensure that spray-men wear shoes and socks.

(7) Each worker should have a broad-brimmed, water-repellent hat. Hats of local manufacture that satisfy these requirements are acceptable and frequently very much cheaper than imported hats.

(8) A veil of plastic netting such as that described by Wolfe et al. (1959) should be attached to the hat in order to protect the face, neck and shoulders of spray-men in those projects where the climate or some other factor prevents the wearing of a plastic face shield. (A visor such as those on caps worn by tennis players does not give adequate protection.)

(9) Rubber gloves are desirable only if they are used properly. Gloves which are contaminated on the inside are a source of added danger rather than protection. The hands should be washed before gloves are put on and gloves should be washed *before* they are removed.

(10) A short (arm-length) cape of plastic sheeting or cotton cloth offers some added protection to the clothed areas beneath it. A cape cannot be considered a substitute for any of the equipment listed under items 1 to 9.

It would be unrealistic to assume that adequate protection can be achieved by substituting bathing for clothing. As already mentioned, the bare head and lower arms provide enough surface for receiving a poisonous dosage of dieldrin in the course of several months of spraying. A larger area of bare skin increases the hazard. If dieldrin reaches the skin, some of it will be absorbed before it can be washed off. Therefore washing and bathing must be an important second line of defence to remove as completely as possible any insecticide which has penetrated the clothing or other protective equipment.

This emphasis on dermal exposure and absorption is not to suggest that dieldrin is not poisonous by other routes. Respiratory toxicity is unlikely to occur only because of the unlikelihood of exposure to a sufficient density of dieldrin-bearing particles 1-5 microns in diameter. The possibility of poisoning from eating dieldrin is much greater than the possibility of

poisoning from inhaling it. It takes only about half as much dieldrin to produce sickness if it is eaten as it does if it is put on the skin. On the other hand, the contamination of the exposed skin of spray-men while they work is inevitable and continuous. The need for protection is not obvious to the ordinary labourer, and even the most practical protective equipment produces some discomfort. By contrast, the need to avoid eating dieldrin is obvious and the means for doing this are simple and involve no real discomfort, although it may take some self-restraint to delay eating, drinking, or smoking until the hands have been washed and until a suitable, uncontaminated place has been found, and it takes a little planning to transport lunches, drinking-water, and tobacco without contaminating them. The possibility cannot be excluded that some cases of occupational poisoning have involved ingestion of dieldrin. However, in studying different programmes it has not been possible to associate poisoning definitely with eating, drinking, or smoking habits. Finally, as already mentioned, the measured contamination of the skin is adequate to explain the observed clinical result.

In the present limited state of knowledge, it seems only reasonable that a person who has shown dieldrin poisoning once should have no further contact with the compound. He should, however, be followed medically for a minimum of two years to determine whether he will show any sequelae. A much longer follow-up is, of course, desirable. It should be noted that all the human cases which have been well described were of the type which, in animals, show spontaneous recovery (albeit with occasional recurrences) without medication. This does not mean that patients should not receive medication. On the contrary, there is evidence that the comfort (if not the survival) of patients can be improved by the same kind of medication which can mean the difference between life and death in more severe poisoning by dieldrin in animals. The treatment includes barbiturates and a proper diet. Phenobarbital is the drug of choice because of its long action; patients should be given as much of this drug as they will tolerate without sleeping more than the usual amount. The diet should be a good one given in sufficient amount to maintain or even increase the body weight.

In addition to protective measures which apply to the individual worker, other factors need to be taken into account:

(1) Sprayers must be kept in repair so that they do not leak.

(2) Measuring cups, mixing buckets, funnels and other devices must be provided with handles which will permit the workers to use them without ever touching dieldrin powder or suspension.

(3) Sprayers should be used at the lowest pressure consistent with vector control. Wolfe et al. (1959) have shown that the contamination of the worker is much greater at a pressure of 50 p.s.i. (3.5 kg per cm^2) than at 20 p.s.i. (1.4 kg per cm^2).

(4) At least one professional man should be appointed safety officer, with no other responsibility and with full power to enforce regulations. The appointment of such an officer will greatly support the authority of foremen who accompany spray-men during the entire working day. It is understood that discipline cannot be adequate unless each spray-man is subject to summary discharge if he violates safety rules and unless each foreman is also subject to discharge for failure to carry out his duty in regard to safety.

(5) Spray-men and mixers should not be permitted to work more than eight hours per day or 40 hours per week.

(6) It must be frankly admitted that (in terms of wall area covered and excluding the cost of insecticide) it is more expensive to apply dieldrin safely than to apply an insecticide like DDT safely. Increasing the pay of spray-men would improve their morale and help to ensure their co-operation in safety regulations.

There is an urgent need for further study of dieldrin to clear up some of the uncertainties which now exist about this very useful insecticide. It is not known how long is required for a single species to reach equilibrium of dieldrin storage. This information is needed to explain the relationship between dieldrin storage and toxicity. It might throw light on the recurrence of symptoms after cessation of dosage and also clarify the hypothesis about allergy to dieldrin. Species may differ widely in the rate at which they reach a steady state in the storage of a compound. Thus, the information on storage is needed eventually in relation to man himself.

Although a method exists for the measurement of dieldrin in fat, methods are not available for measuring dieldrin or any derivative in the blood or the excreta. Such methods should be devised, if possible. The appropriate measurement of dieldrin-derived material in the blood or urine of spray-men should give information on:

(*a*) the relative amount of dieldrin absorbed under different conditions of spraying;

(*b*) the time necessary to reach an equilibrium of excretion; and thus

(*c*) the relation between toxicity, dosage, and time.

Especially in view of the present lack of a method for measuring dieldrin in blood or excreta, it would be highly desirable if measurements similar to those reported by Fletcher et al. (1959) could be made in a number of dieldrin-spraying programmes. It is true that Wolfe et al. (1959) have measured the effectiveness of protective clothing and devices employed by a single skilled spray-man. However, similar information should now be obtained under a variety of field conditions involving differences of climate, labour force, etc. It is entirely possible that study of such measurements would make it possible to state with greatly increased confidence that certain spray practices are safe.

It has been claimed that by clinical histories and neurological examinations done at intervals, it is possible " to detect incipient intoxication by dieldrin before serious manifestations occur " (Winthrop & Felice, 1957). The possibility is a very attractive one, worthy of the most careful scientific work to confirm or refute it. Unfortunately, the conditions of such a study are complex. It is necessary that the investigators be versed in statistical tests of probability as well as in clinical medicine. It is also necessary that a programme be selected for study which has given rise to a significant incidence of poisoning in the past and in which the initial conditions of exposure of the workers can be continued without change during at least two years of investigation. Of course, if cases of clinical poisoning continued to appear under these conditions, the limited usefulness of the test would be revealed in a shorter time.

RÉSUMÉ

La dieldrine est de plus en plus utilisée dans la lutte contre le paludisme pour plusieurs raisons, dont une est la résistance sporadique au DDT de quelques vecteurs. L'intoxication par la dieldrine des hommes qui vaporisent cet insecticide a été observée en Equateur, en Inde, au Nigeria, au Venezuela et plus récemment en Indonésie. D'autres cas ont été signalés dans plusieurs autres pays. L'auteur décrit quelques cas d'intoxication en Indonésie.

Les risques liés à l'utilisation de la dieldrine sont proportionnels au degré d'exposition des travailleurs, lui-même déterminé par la concentration, la surface cutanée dénudée, le temps de contact et le manque d'hygiène: tels sont les enseignements des programmes de lutte antipaludéenne au Kenya, au Tanganyika, en Indonésie, dans l'Etat de Bombay, en Iran et ceux de la littérature s'y rapportant. Si les risques d'inhalation de dieldrine sont insignifiants dans les conditions habituelles de travail, si l'ingestion en est dangereuse, et tout travailleur comprend bien qu'il faut l'éviter, par contre la nécessité d'éviter l'exposition cutanée n'a pas été assez bien comprise, même par les dirigeants des programmes de lutte. Les moyens de mesurer l'exposition des travailleurs à la dieldrine et les recherches sur les différentes voies possibles d'intoxication montrent que la contamination par la peau constitue en pratique le danger le plus grand. Le produit est à peine plus toxique par la bouche que par application cutanée. La peau absorbe avec autant de facilité la dieldrine en poudre que la dieldrine en solution. La toxicité orale de la dieldrine est seulement trois à cinq fois plus forte que celle du DDT. Cependant, le DDT n'est pas facilement absorbé par la peau, même en solution, et le DDT en poudre est si peu absorbé de cette façon que sa toxicité par cette voie n'est pas patente.

Si l'on suppose que l'homme est aussi sensible à la dieldrine que les animaux de laboratoire, le nuage «imperceptible» de dieldrine qui adhère au visage non protégé et sur les avant-bras des hommes qui vaporisent est suffisant pour expliquer la fréquence des intoxications observées. Ceci n'est pas étonnant quand on pense qu'au cours d'une journée de travail le nuage de vaporisation, s'il est imperceptible quand il retombe, finit par couvrir la peau d'une pellicule bien visible.

La dieldrine ne doit donc pas être utilisée à la légère; si son utilisation est indispensable, des mesures individuelles et collectives de protection peuvent diminuer les risques, sans forcément les éliminer. Il faut donc dire à chaque travailleur les dangers de la dieldrine et la nécessité d'une collaboration de sa part dans les mesures de protection. Il faut surveiller le lavage *a*) des mains à intervalles fréquents, *b*) des mains et du visage avant les repas ou avant de fumer, *c*) de toute surface cutanée visiblement atteinte, *d*) de tout le

corps après le travail. Il faut exiger ou procurer *a*) du savon à discrétion, *b*) une lessive quotidienne des vêtements de travail, *c*) au moins deux jeux de vêtements (uniquement destinés au travail) à col montant assez haut, à manches longues et à pantalon long, *d*) un chapeau à larges bords, *e*) un voile en filet de plastique comme ceux décrits par Wolfe et al. pour les programmes de lutte où un masque en plastique ne peut être utilisé du fait du climat ou pour d'autres raisons. Des gants en caoutchouc ne sont souhaitables que s'ils sont utilisés à bon escient. Une courte pèlerine peut augmenter la protection des vêtements qu'elle recouvre. Enfin, à ces mesures, il faut ajouter l'entretien des pulvérisateurs et la nécessité de munir de poignées les récipients de mesure, les seaux et autres ustensiles que les travailleurs doivent pouvoir manipuler sans toucher à la dieldrine. La pression des pulvérisateurs sera la plus basse possible, compatible avec la lutte contre les vecteurs. On devrait toujours désigner un responsable de la sécurité, le travail ne devrait durer que huit heures par jour et 40 heures par semaine. Il faut d'autre part tenir compte franchement des dépenses supplémentaires qu'entraîne l'utilisation en toute sécurité de la dieldrine. Il est urgent d'entreprendre des études complémentaires sur la dieldrine, notamment pour éclaircir certaines incertitudes que comporte encore cet insecticide, pourtant des plus utiles. Il faudrait en particulier *a*) étudier la dynamique d'accumulation de la dieldrine dans n'importe quelle espèce et par la suite chez l'homme, *b*) mettre au moint une méthode quantitative de mesure de la dieldrine, ou d'un dérivé, dans le sang et les urines de l'homme, *c*) trouver les moyens supplémentaires de mesurer le degré d'exposition des hommes qui vaporisent, dans les différentes conditions de travail et *d*) faire une étude critique de la valeur de certains procédés de diagnostic des intoxications légères ou imminentes.

REFERENCES

Blazquez, J. & Bianchini, C. (1956) *Gac. méd. Caracas*, **63**, 1

Blazquez, J. & Bianchini, C. (1957) *Bol. Ofic. sanit. panamer.*, **43**, 121

Fletcher, T. E., Press, J. M. & Bagster Wilson, D. (1959) *Bull. Wld Hlth Org.*, **20**, 15

Hayes, W. J., jr (1957) *Publ. Hlth Rep. (Wash.)*, **72**, 1087 (Also in *Bol. Ofic. sanit. panamer.*, **43**, 534)

Hayes, W. J., jr, Ferguson, F. F. & Cass, J. S. (1951) *J. trop. Med. Hyg.*, **31**, 519

McMahon, J. (1957) *E. Afr. med. J.*, **34**, 507

Patel, T. B. & Rao, V. N. (1958) *Brit. med. J.*, **1**, 919

Rahman, J., Singh, M. V. & Datta, S. P. (1958) *Bull. nat. Soc. India Malar.*, **6**, 107

Winthrop, G. J. & Felice, J. F. (1957) *Bol. Ofic. sanit. panamer.*, **43**, 512

Wolfe, H. R., Walker, K. C., Elliott, J. W. & Durham, W. F. (1959) *Bull. Wld Hlth Org.*, **20**, 1

World Health Organization, Study Group on the Toxic Hazards of Pesticides to Man (1956) *Wld Hlth Org. techn. Rep. Ser.*, **114**