

this in children and young adults; the corresponding rate for the autumn of 1918 was probably at least ten times as high. The overwhelming preponderance of staphylococci in the 1957 epidemic also stands in contrast with the prevalence of *H. influenzae*, and to a less extent haemolytic streptococci and pneumococci, in 1918.

The pathogenic significance of the bacterial invaders in influenza has been debated, but so far as *Staph. aureus* is concerned its pathogenicity in other situations is not doubted. In this series virtually no deaths occurred in children or young adults in the absence of *Staph. aureus*, whereas in the very young and the old, in whom milder infections might well be fatal, staphylococci were less often found. The small group of patients with rheumatic heart disease perhaps fall into the same category. It seems impossible to believe that a heavy and extensive growth of pathogenic staphylococci in the lungs was not responsible for most of the deaths in young healthy persons in this epidemic. It is clear that *H. influenzae*, despite its prominence in the past, did not play an important part in 1957, even though technical difficulties may have led to some underestimate of its frequency.

Except in older people, there was no evidence that the staphylococci were often acquired in hospital; but whether they came from the patient himself or his contacts and environment, or whether from healthy carrier sites or septic lesions, is unknown. Attempts to find a history of sepsis in the patient or his contacts were unsuccessful.

It is impossible to say whether various methods of treatment that failed in these patients were successful in others, but it is evident that the earliest signs of pneumonia in patients with influenza must be regarded as potentially having the gravest significance, requiring urgent treatment. Broad-spectrum antibiotics should probably be given parenterally, while corticosteroids and staphylococcal anti-toxin deserve a trial.

Summary

Records of 477 patients who died from pneumonia in the 1957 epidemic of Asian influenza were obtained from laboratories throughout the country. Influenza virus A of Asian type was isolated from 195 of 310 specimens tested.

The most striking feature of the illnesses was the speed with which the patients deteriorated and died after admission to hospital. The duration of illness increased with age; 60% of children under 5 died within 48 hours of onset, but only 10% of those over 45. Pneumonia—often haemorrhagic—tracheobronchitis, and lung abscess were the most frequent post-mortem findings.

Staphylococcus aureus was found in lung or sputum specimens from 62% of the patients. Other pathogenic organisms were reported in 8%, and the remainder yielded no pathogenic organisms or were sterile. Staphylococci were found less frequently in young children (49%) and old persons (31%); and most frequently in children of school age (88%).

Although only 65% of staphylococci isolated from patients not admitted to hospital or dying within 48 hours of admission were sensitive to penicillin, most infections, except in old people, were acquired outside hospital.

The records were contributed by pathologists from at least 112 hospitals and 24 public health laboratories; they were analysed, and this report prepared, at the Central Public Health Laboratory, Colindale, by Dr. J. C. McDonald and Dr. R. E. O. Williams.

REFERENCE

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"DIELDRIN" POISONING IN MAN A REPORT OF 20 CASES OBSERVED IN BOMBAY STATE

BY

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Reports of cases of poisoning in men using insecticides for the control of diseases such as malaria and filariasis are comparatively rare. Workers engaged in the industrial production of insecticides, though exposed to a potentially greater hazard, are usually well protected by suitable safety measures. Although the risk to field-workers may be less, cases of poisoning due to carelessness have been recorded.

Bombay State was one of the first States to use insecticides for the control of malaria over large areas, so that with the introduction of the National Malaria Control Programme it has been possible to cover every malarious village in the State. Filariasis is less widespread within the State, but the programme has resulted in its effective control.

The insecticides originally used for control of malaria were D.D.T. and B.H.C., but recently dieldrin has been introduced for indoor residual spraying. Only dieldrin has been used in the filaria control work.

In both programmes a 50% dieldrin wettable powder is used, but the strength of the final diluted suspension is 1.25% for malaria control and 2.5% for filaria control work. The rate of spraying is the same in both cases, and the deposits are 28 and 56 mg. per sq. ft. (290 and 580 mg. per sq. metre) respectively.

Incidence of Cases

During the years that D.D.T. and B.H.C. were used no cases of poisoning were observed in the spray teams. This paper describes 20 cases of poisoning by dieldrin among the men applying this insecticide in spray programmes. The cases occurred in 1957 in two units in widely separated areas. They were the Filaria Control Unit in Nagpur (10 cases) and the Malaria Control Unit in Thana (10 cases). Dieldrin has been used for the past two years in Poona District, but no cases of poisoning have been recorded from there. The spraying programmes are illustrated in Figs. 1 and 2. There were approximately 105 workers applying the stronger concentration in the filaria unit, and 10 cases of poisoning were observed amongst them. It is possible that some earlier cases were missed before the association of dieldrin with the clinical syndrome had been established. The malaria unit numbered 192 workers, and there were 10 cases of poisoning among these men, roughly half the incidence of that in the filaria unit.

Relation to Exposure

In the filaria unit poisoning was seen from 14 to 154 days (average, 57 days) after the first exposure to dieldrin (Fig. 1). In one case severe symptoms first developed 15 days after exposure had ceased, though milder symptoms had apparently been noted earlier. In another case there had been no exposure for eight months, but the patient had a fit while he was engaged in spraying B.H.C.

In the malaria unit the period of exposure was longer but only one of the 10 cases had symptoms during the first period of exposure. The rest occurred early in the second

phase, which followed after a month's interval. In the malaria unit the cases occurred from 60 to 116 days (average, 99 days) after exposure had started (Fig. 2).

In 19 of the cases there was a history of having been engaged in either preparing or spraying dieldrin suspensions. The other patient had sprayed for a short period before taking over supervisory work.

The spraying teams were accustomed to the use of D.D.T. and B.H.C. and had been in the habit of using their bare hands both for transferring the powder from the containers to the water and for stirring the suspensions prepared from the powders. No protective clothing or masks were used, and washing with soap and water was not introduced until later.

Clinical Features

The case histories were all personally recorded by one of us (V.N.R.), care being taken to avoid leading questions. All patients were males aged 16 to 40 years. The symptoms show a definite gradation, starting with giddiness, headache, and twitching of muscles and going on to convulsive attacks occurring up to several times a day, with loss of consciousness for periods of up to two hours. There have been no deaths. The cases in the malaria unit were less severe than those in the filaria unit. Whereas every case in the latter team had convulsions ranging from a single one to very

many, in the malaria unit only 6 out of the 10 cases had fits, the maximum number of fits being four.

The convulsions were similar to epileptic fits, but they were never preceded by any sensory disturbance or aura. In six cases there was a history of giddiness before the attack. The fits occurred at any time of the day or night, and were not associated with emotional or other disturbances. In two cases there was a history of fits occurring during sleep. Fits were characterized by violent tonic contractions of the body muscles, rolling up of the eyeballs, clenching of the teeth, and occasional tongue-biting. There was no periodicity in the occurrence of the fits. Psychic disturbances ranging from loss of memory for recent events to serious disturbances such as mania have been observed. Symptoms such as loss of weight, loss of appetite, fatigue, weakness, etc., have not been definite enough for any importance to be attached to them. There was a loss of weight and appetite, however, in Cases 5 and 9, and of weight in Case 7. Cases 4 and 9 had some loss of memory, the latter case also showing maniacal symptoms. There was no family history of epilepsy in any of the cases.

Differential Diagnosis.—This rested mainly on the history of exposure to dieldrin and an absence of any clinical history of fits occurring before such exposure had taken place. There is an absence of an "aura" and periodicity in the attacks.

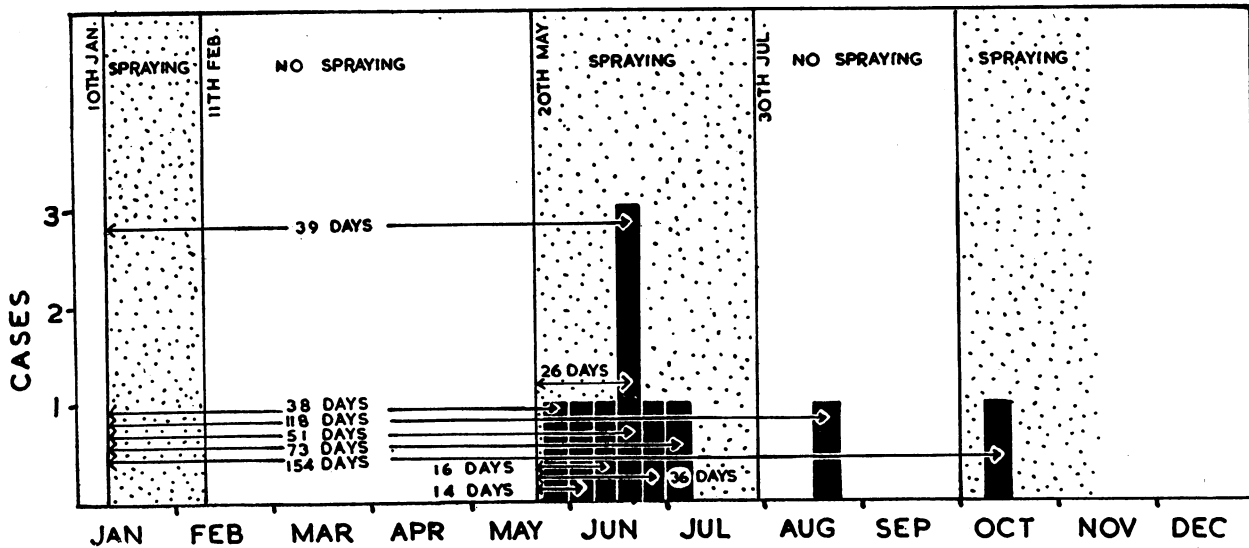


FIG. 1.—Filaria control unit, Nagpur. Occurrence of dieldrin toxicity cases in relation to time of spraying and duration of exposure in 1957. The final dilution of dieldrin suspension was 2.5%. (Note: The days of exposure shown represent the total period of exposure in the first and second rounds of spraying. It is necessary to remember that exposure was not continuous and there were clear periods of non-exposure of varying duration.)

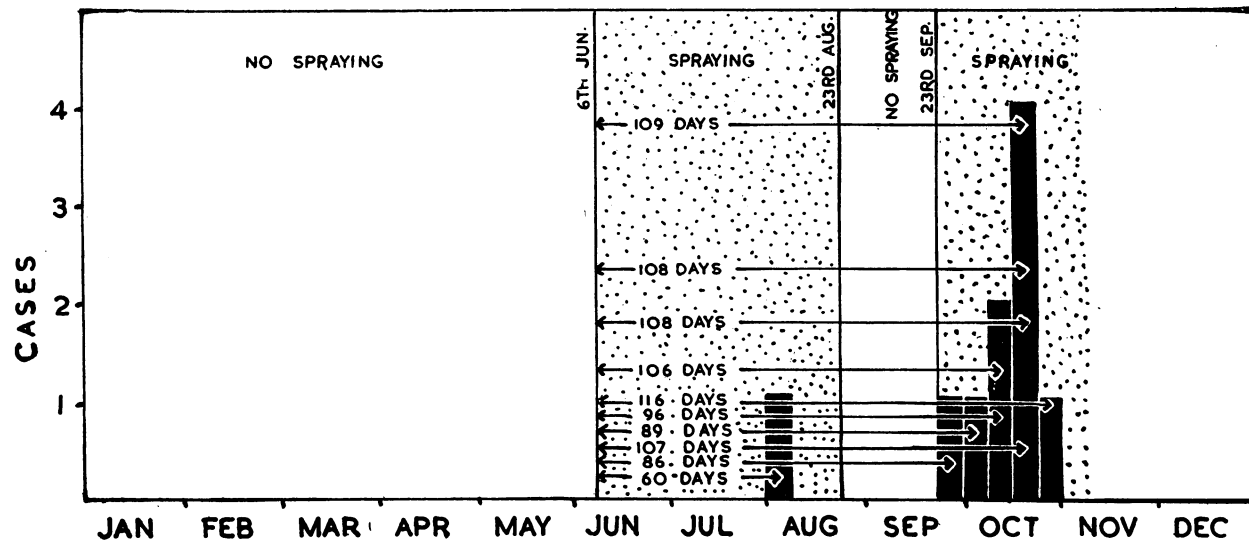


FIG. 2.—Malaria control unit, Thana. Occurrence of dieldrin toxicity cases in relation to time of spraying and duration of exposure. The final dilution of dieldrin suspension was 1.25%. (Note as Fig. 1.)

Details of 20 Male Cases of Dieldrin Toxicity

Case No.	Age	Characteristics of Fits and Muscular Contractions				Symptoms During an Attack of Fit								
		Occurrence of Fit in Relation to Period of Exposure	Total No. of Fits	Duration of Fit	Muscular Twitching	Complete Loss of Consciousness	Tonic Contraction of Muscles	Clenching of Jaws and Occasional Biting of Tongue	Frothing from Mouth	Rolling up Eyeballs	Giddiness	Head-ache	Vomit-ing	Weak-ness and Fatigue
<i>Nagpur District</i>														
1	22	30* days	Many	1½ hrs.	+++	+++	+++	Nil	+++	+++	Nil	+	Nil	Nil
2	16	20* "	2	Short time	++	+++	+++	++	+++	+++	++	+	Nil	Nil
3	19	86* "	3	½ hr.	+++	+++	Nil	+++	Nil	+++	++	++	++	++
4	21	?	2	½ "	Nil	+++	+++	+++	+++	+++	++	++	++	++
5	20	8* "	4	15 mths.	..	+++	+++	+++	+++	++	+++	++	++	+++
6	22	28* "	1	½ hr.	..	+++	Nil	+++	+++	++	+++	++	++	Nil
7	30	14* "	5	2 hrs.	+	+++	+++	+++	+++	++	Nil	++	++	+++
8	40	?	2	?	Nil	+++	Nil	+++	+++	++	+++	++	+	+++
9	40	15* "	2	1 hr.	..	+++	+++	+++	+++	++	+++	++	Nil	Nil
10	19	30* "	5	1-2 hrs.	..	+++	+++	+++	+++	++	+++	++	++	++
<i>Thana District</i>														
11	19	16* "	1	15 mths.	+++	+++	+++	+++	Nil	..	+++	+++	++	..
12	21	4* "	2	1½ hrs.	Nil	+++	Nil	Nil	++	++	+++	+++	++	..
13	22	23* "	1	½ hr.	..	+++	+++	+++	..	+++	Nil	+++	+++	++
14	20	28* "	Nil	Nil	Nil	Nil	..	+++	+++	+++	+++	++
15	24	27* "	1	½ hr.	..	+++	+++	+++	..	+++	Nil	+	+++	++
16	23	28* "	2	1½ hrs.	..	+++	+++	+++	..	+++	Nil	+	+++	++
17	20	8* "	1 (?)	Momentary	+++	+++	Nil	+
18	23	64 (1st round)	4	½ hr.	Nil	+++	+++	+++	Nil
19	27	28	4	20 mths.	+++	+++	+++	Nil	++?
20	21	5* "	Nil	..	+++	+++	Nil	+++

* Duration of exposure calculated from the commencement of second round of spraying of dieldrin as the cases occurred during the second round only.

Mode of Action of Dieldrin

Nothing yet is known about the mode of action of dieldrin and the related group of chlorinated hydrocarbon insecticides. They are all capable of causing nervous excitation, with twitching and convulsions presumably due to some irritant action on nerve cells. These cases are particularly interesting because they occurred only after a long period of exposure. Three possibilities can be envisaged: (1) A prolonged cumulative effect, with clinical manifestations finally brought about by a single heavy dose exceeding the threshold for the excretion or detoxication of dieldrin in the body. (2) A cumulative deposition of dieldrin in the system liable to be reactivated by physiological or functional change in the body. (3) Allergic manifestations.

The occurrence of cases after a fairly long period of exposure is rather suggestive of a cumulative effect of the poison. But the occurrence of typical fits after a short period of exposure of 14 to 36 days in four cases suggests the possibility that cases occur within a short period of time with heavy doses of dieldrin. The dose of the insecticide appears to be of prime importance. The possibility of its being deposited in the body in an inactive form with the body fat, as is largely believed, with capability of reactivation under conditions of physiological or functional stress, cannot be ruled out.

The occurrence of one case in the Filaria Control Unit, Nagpur (Case 3), 15 days after withdrawal from exposure to dieldrin can thus be explained. However, the occurrence of most of the cases some time after the first exposure and during a short period of second exposure to dieldrin, together with the occurrence of cases after cessation of exposure, suggest that toxic manifestations denote an allergy to dieldrin. Drug allergy is well known. Allergic manifestations as a result of combination of the insecticides with protein have also been recognized. The absence of skin reactions and symptoms referable to joints in our cases is worth mentioning. The toxic manifestations observed in one patient (Case 4) who came into direct contact with dieldrin only in the months of January and February, and who had a fit in October—that is, eight months later—while supervising B.H.C.-spraying work, strongly support the possibility that fits are an allergic manifestation. The precipitation of a fit after exposure to B.H.C., another chlorinated hydrocarbon, is of particular significance with reference to allergy.

At this juncture it is very difficult to say with any degree of certainty by what exact mode of action dieldrin produces

toxic manifestations: more than one of the possible modes of toxic action suggested above is presumably operating.

The elimination of dieldrin either by detoxification by the liver or by excretion through the kidney is also a matter of importance. The cumulative action of the insecticide is largely dependent upon how far it is eliminated. That cases occur after exposure to dieldrin is discontinued suggests the possibility of cumulative action as a result of slow elimination or the deposition of dieldrin in an inactive form with potentialities for reactivation at a later date under certain circumstances, as already postulated.

It is realized that more detailed clinical, biochemical, and laboratory examination is necessary to arrive at more specific conclusions. A few cases are being studied in great detail with this point of view, and a further communication will follow.

Route of Absorption

Dieldrin may be absorbed by the dermal, oral, and respiratory routes, as shown in experimental animals. The use of bare hands for carrying the powder and preparing the water suspensions, together with the continued use of working clothes for two to three days at a time, would undoubtedly favour absorption through the skin. Ingestion of dieldrin could have taken place by transfer to food from unwashed hands, and inhalation could have occurred among those engaged in spraying operations.

The exact importance of any particular route is difficult to assess, but it is hoped that the incidence of poisoning will be reduced by the introduction of suitable precautions.

Summary

An account is given of 20 cases of poisoning by dieldrin among spray teams in malaria and filaria control work. Though convulsions were seen in the majority there were no deaths.

The incidence of poisoning in relation to exposure is described and most cases occurred during a second period of exposure. In one patient the first convulsion was noted 15 days after the last exposure.

Handling dieldrin powder and stirring suspensions with bare hands, and inadequate general hygienic measures, may be important factors in determining the incidence of these cases.