Int Arch Occup Environ Health (1981) 48:301–308

International Archives of
Occupational
and
Environmental
Health

Long-Term Occupational Exposure to DDT*

M. K. J. Siddiqui[1], M. C. Saxena[1], U. K. Mishra[2], C. R. Krishna Murti[1], and D. Nag[2]

[1] Industrial Toxicology Research Centre, Post Box No. 80, Lucknow-226001, India
[2] Department of Neurology, King George's Medical College, Lucknow

Summary. Blood serum of twenty workers occupationally exposed to DDT for an average duration of 14 years was analysed for organochlorine pesticides by gas-liquid chromatography with an electron capture detector. Significant levels of BHC, p,p'-DDT, p,p'-DDD and p,p'-DDE were detected. A higher incidence of total DDT equivalent, about 10 times, was observed in DDT exposed workers when compared with a comparable sample of unexposed persons from the general population. Levels of DDT in serum of occupationally exposed workers were more than the permitted level of 200 ppb. The daily intake was computed to be about 10 mg/man/day as against 0.25 mg—the acceptable daily intale. Abnormal nerve conduction was encountered in a few cases of DDT sprayers. No significant correlation was observed between the total DDT equivalent in serum and duration of occupational exposure in workers. Levels of BHC in controls was 2.3 times the level in exposed workers, possibly due to induction of hepatic drug metabolising enzymes by high levels of DDT in the latter group. Findings are discussed in the light of existing knowledge of the bio-chemical effects evoked due to residual intoxication of DDT during occupational exposure.

Key words: DDT – BHC – Nerve conduction – Hepatic microsomal drug metabolising enzymes – Accepted daily intake

Introduction

The widespread use of dichlorodiphenyltrichloroethane (DDT) in Indian agriculture and in vector control programmes and its ability to pass on into the food chain has caused the dangers of DDT build up in the environment as well as in human tissues to be a public health issue in this country. Indians have been reported to carry the highest body burden of pesticides [2]. All these rendered essential the study of the effects of DDT on man, particularly in relation to occupational exposure.

Offprint requests to: M. K. J. Siddiqui (address see above)

0340-0131/81/0048/0301/$ 1.60

A number of assessments of human health in populations exposed to DDT have been made [1, 5, 6]. Among the most important are the studies on occupationally exposed workers whose daily contact with DDT far exceeds that of the general population [10, 15, 20]. The study of such workers and unexposed volunteers [4, 7, 11, 12, 18] provides an index of the limits and effects of human exposure. Study of workers chronically exposed to high levels of DDT over long periods can also be an indicator of time-dependent effects on the general population. The aim behind this investigation was to monitor the health of workers regularly in contact with DDT. In addition to recording the general health status, estimates of the concentrations of organochlorine pesticides, DDT and its metabolites and benzenehexachloride (BHC) were made in the sera of workers occupationally exposed to DDT and in a control population (having no accidental/occupational exposure).

Materials and Methods

Twenty subjects engaged in spraying DDT under a plant protection programme around Lucknow were studied. The age of the subjects ranged from 25 to 52 years, with a mean of 40 years. The duration of exposure to DDT in their occupation ranged from 1 to 32 years, with mean of 14 years. All were asked to complete a detailed questionnaire related to appearance of clinical signs due to DDT intoxication such as headache, dizzines, nausea, vomiting, pain, numbness of the limbs and general weakness. Measurement of their nerve conduction velocities was also carried out. Their age, dietic habits, ethnicity (rural/urban) and duration of exposure were recorded. Five ml blood were collected by veni puncture in pre-heparinized vials. The same amount of blood was also collected from 15 human subjects from the blood bank of King George's Medical College, Lucknow. The blood donors did not reveal any past history of accidental or occupational exposure to any of the pesticides. These donors were treated as controls.

Blood was centrifuged at 2000 rpm for 5 min in a refrigerated centrifuge to separate the serum. Extraction and clean-up of the serum was carried out according to Dale et al. [3]. One ml of the blood serum was taken in a clean dry 25 ml conical flask, 5 ml of formic acid and 3 ml of hexane added and shaken for 1 h at 37° C in a mechanical shaker. Loss of n-hexane during shaking was made up by weighing the flask before and after shaking.

The contents were then transferred to graduated centrifuge tubes and the hexane layer was taken out with the help of a disposable suction pipette. Clean-up of the extract (hexane) was done by treating it thrice with fuming sulphuric acid and a layer was then collected for analysis using a gas-liquid chromatograph. Recoveries in excess of 92% were observed for all the pesticides in the fortified samples.

All samples were analysed by gas-liquid chromatography (GLC) using a Varian Aerograph series-2400 equipped with an electron capture detector. The following conditions were used for the analysis.

Carrier gas	purified nitrogen (99.9%) passed through silica gel and molecular sieve to remove moisture and oxygen, respectively.
Gas pressure	65 p.s.i.
Flow rate	45 ml/min
Injector temperature	190° C
Column temperature	180° C
Detector temperature	200° C
Attenuation	4×10^{-9}
Current	10^{-9} μA
Column	Glass spiral column of length 6 ft packed with gas chrome Q coated with 1.5% OV-17 + 1.95% OV-210.
Detection limits in ppb	α-BHC 1, β-BHC 1, γ-BHC 1, p,p′-DDE 1, p,p′-DDD and p,p′-DDT 2.
Sample size	4 μl to 8 μl

Standards were obtained from Poly-Science Corporation, Illinois, USA.

The chemical nature of residues detected were confirmed by comparing Rf value of samples with those of standards by Thin-layer chromatography.

Results

Results are summarized in Tables 1 to 5. Table 2 represents the frequency of distribution of DDT, its metabolites and BHC.

It is of paramount importance to mention here that the case history of the subjects occupationally exposed to DDT did not report their occupational/accidental exposure to BHC. Therefore, the levels of BHC estimated in both the control and DDT exposed subjects are presumably representative of intake through food. However, their possible entry through respiratory or dermal route from the polluted environment is not altogether ruled out.

From results presented in Table 3 it is seen that p,p'-DDE levels in DDT exposed workers are 8 times higher than those of controls and levels of p,p'-DDT are 6 times as high as in controls. However, on the basis of total DDT residues, exposed subjects show 10.7 times more than control subjects.

Table 1. General survey of the workers

No.	Occupation	Age (years)	Duration of exposure (years)	Nerve conduction velocity (m/s)
1.	Sprayer	25	10	54.5 and 49
2.	Sprayer	45	20	58.8 and 38[a]
3.	Sprayer	31	8	58.3 and 45
4.	Vehicle carrier	52	32	52 and 46.1
5.	Sprayer	50	31	52 and 46.1
6.	Sprayer	40	20	46.6 and 29[a]
7.	Sprayer	46	18	60.5 and 50
8.	Sprayer	45	17	61.1 and 44.6
9.	Sprayer	42	24	60 and 51
10.	Sprayer	48	16	70 and 38.2[a]
11.	Sprayer	35	6	65 and 52
12.	Sprayer	40	10	62 and 51
13.	Sprayer	39	10	53 and 47
14.	Sprayer	52	6	52 and 46.4
15.	Sprayer	29	1	55 and 51
16.	Sprayer	34	14	56 and 41
17.	Sprayer	34	8	60 and 50
18.	Sprayer	35	17	52 and 46.2
19.	Sprayer	45	20	54 and 49
20.	Sprayer	40	14	58 and 45

Ethnicity of the workers was not given in the table as they were all urban residents

[a] Abnormal nerve conduction

Table 2. Frequency of distribution of detected pesticides in control subjects and in workers occupationally exposed to DDT

Pesticides estimated	15 control subjects		20 DDT exposed workers	
	No. of + Ve individuals	% + Ve	No. of + Ve individuals	% + Ve
BHC	15	100	20	100
Lindane	15	100	20	100
p,p'-DDE	15	100	20	100
p,p'-DDD	8	51	17	85
p,p'-DDT	13	82	20	100
Σ DDT	15	100	20	100

BHC represents sum of its α, β and γ-isomers (lindane)
Σ DDT = Total DDT equivalent (Sum of isomers of DDT and their metabolites equivalent to DDT)

Table 3. Levels of DDT and its metabolites in control subjects and in workers occupationally exposed to DDT in ppb

Pesticides	Control	DDT exposed workers	Ratio of exposed to control
	Range (Mean ± S.D.)	Range (Mean ± S.D.)	
p,p'-DDE	8 – 60 (19 ± 12)	28 – 320 (152 ± 86)	8
p,p'-DDD	n.d. – 99 (21 ± 15)	n.d. – 99 (32 ± 28)	1.5
p,p'-DDT	n.d. – 81 (32 ± 24)	9 – 548 (203 ± 94)	6.3
Σ DDT	30 – 120 (38 ± 29)	43 – 791 (409 ± 196)	10.7

Subjects	Total BHC	Lindane
Control	21 – 270 (131 ± 105)	8 – 47 (25 ± 16)
Exposed	11 – 150 (55 ± 41)	6 – 28 (11 ± 6)
Exposed/Control ratio	0.41	0.44

Table 4. Levels of BHC in control subjects and in workers occupationally exposed to DDT in ppb

Table 5. Percentage metabolism of DDT estimated as DDE and DDD in control subjects and in DDT exposed workers

Metabolite	Control	DDT exposed workers	% change
p,p'-DDE	50	37	26
p,p'-DDD	55	8	84

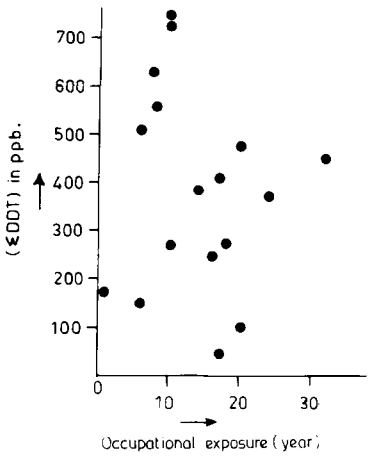

Fig. 1. Concentration of total DDT equivalent in blood sera of spraymen plotted as a function of duration of their occupational exposure in years

Levels of BHC to which neither controls nor DDT exposed workers were occupationally/accidentally exposed are given in Table 4. It is to be noted that BHC levels are 2.3 times higher in controls as compared to DDT exposed workers. The same ratio holds good for lindane between the two groups of volunteers.

Assuming that all the DDE and DDD was formed as a result of metabolic degradation of DDT inside the human subjects and neither the controls nor the exposed subjects were exposed to DDE through air/water/food chain contamination, Table 5 depicts a comparison of the metabolic rates of DDT in control subjects and in DDT-exposed workers, showing that the rate of biodegradation from DDT to DDE in normal and exposed workers is almost the same, however, that of DDT to DDD is significantly higher in controls than in DDT exposed workers.

None of the subjects reported any typical signs of DDT intoxication.

Efforts were made to find out the correlation, if any, between the duration of occupational exposure and levels in the blood serum of workers by plotting levels of total DDT equivalent in the serum as a function of their occupational exposure in years (Fig. 1) but did not reveal any relationship. In Fig. 1 there are 17 points as against 20 workers plotted because 4 workers retained the same residue level and had the same exposure time. Figures 2 and 3 show chromatograms of a normal and a DDT exposed blood serum, respectively.

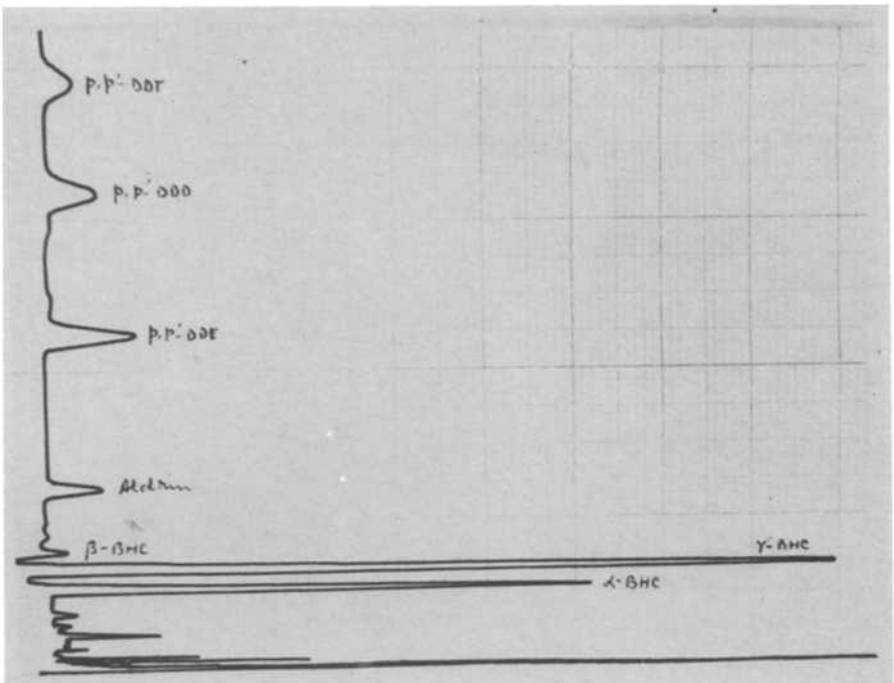

Fig. 2. Chromatogram of normal blood serum

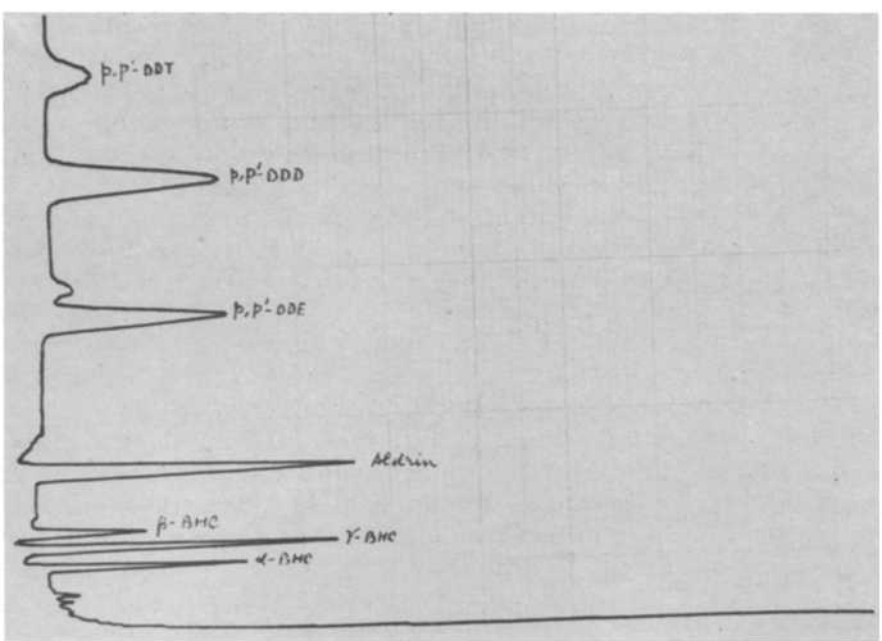

Fig. 3. Chromatogram of blood serum of a DDT-exposed worker

Discussion

A survey of 144 spraymen associated with malaria control in India by the World Health Organisation [21] revealed that blood levels of DDT were 7.5–15 times those in controls and were at least as high as those reported for workers who manufacture and formulate DDT elsewhere in the world. On examination they showed brisker knee reflexes and slight tremor was more often present. In the present study confined to only twenty spraymen with different exposure periods, total DDT residues were about ten times those in controls. Workers did not report any untoward signs on clinical examination. DDT sprayers having total DDT residues of 478, 107 and 249 ppb in their serum showed abnormal nerve conduction i.e. 58.8 and 38, 46.6 and 29 as well as 70 and 38.2 m/s respectively. However, this abnormality cannot be solely attributed to DDT because the subjects with 791, 633 and 510 ppb also showed normal nerve conduction.

Zielhuis [22] suggested levels below 200 ppb of total DDT in the blood as No Effect Level (NEL). It was however recommended that when the range is 200–500 ppb the worker should be temporarily removed from his occupation.

Further, according to Poland [16] an average level of 573 ppb DDT in blood of the exposed workers corresponds to an average daily intake of about 18 mg/man/day. Since in the present study the average was 409 ppb of DDT equivalent in the occupationally exposed workers, their average daily intake is about 10.3 mg/man/day against 0.25 mg/man/day, the acceptable daily intake (ADI) recommended by WHO/FAO.

DDT has been shown to cause the induction of hepatic drug metabolising enzymes (HDME) in man [16, 17]. Increased metabolism of drugs and steroids indicative of induction of hepatic microsomal enzymes [8, 9] have been reported in workers exposed to DDT. Therefore, considerably low levels of BHC in DDT exposed workers as compared with controls assume a great significance. High levels of DDT in occupationally exposed workers in the present study might have resulted in the induction of HMDME and led to a rapid biodegradation of BHC in the exposed workers.

A significant increase in serum lactic dehydrogenase (LDH) activity (< 0.05) and a more substantial decrease in serum creatine phosphokinase (CPK) activity (< 0.05) in workers with 16–167 ppb of p,p′-DDT in their serum has been reported [13]. A range of 9–548 ppb of p,p′-DDT was observed in the present study.

Morgan and Lawrence [14] showed a negative relationship between serum bilirubin and serum (DDT + DDE) and suggested a continuous reduction in serum bilirubin as a function of serum (DDT + DDE) level over the range which was less than the present study. As an inducer of xenobiotic metabolising enzymes of the liver, DDT (and probably DDE) stimulate the activity of glucuronyl transferase which is responsible for the excretion of bilirubin. It is this effect of DDT which plays an important role in the clinical control of jaundice due to congenital deficiency of hepatic glucuronyl transferase [19].

Control subjects were not individually matched to pesticide (DDT) exposed workers by age, dietic habits and ethnicity. Failure to match subjects individually in the majority of cases limited the sensitivity of this study as an epidemiologic

investigation, because measurements based on unmatched controls can only be used as rough guides with which to compare data from pesticide exposed subjects.

Acknowledgement. Authors are thankful to H. O. Mishra, S. Q. Mehdi, R. K. Hans and G. S. Tondon of the instrumentation section of Industrial Toxicology Research Centre, Lucknow for their sustained help.

References

1. Case RAM (1945) Toxic effects of DDT in man. Br Med J 2:842–845
2. Dale WE, Copeland MF, Hayer WJ (1965) Chlorinated insecticides in the body fat of people. Bull World Health Org 33:471
3. Dale WE, Miles JW, Graines Thomus B (1970) Quantitative method of DDT and DDT metabolites in blood serum. J Assoc Offic Anal Chem 53 [6]:1287
4. Hayes WJ Jr, Durham WF, Cueto C Jr (1956) The effect of known repeated oral doses of chlorophenothane (DDT) in man. J Am Med Assoc 162:890–897
5. Hayes WJ Jr (1967) Toxicity of pesticides to man: risks from present levels. Proc R Soc Lond [Biol] 167:101–127
6. Hayes WJ Jr (1969) Pesticides and human toxicity. Ann Ny Acad Sci 160:40–54
7. Hayes WJ Jr, Dale WE, Pirkle Cl (1971) Evidence of safety of long term, high oral doses of DDT for man. Arch Environm Health 22:119–135
8. Kolmodin-Hedman B (1973a) Decreased plasma half-life of phenylbutazone in workers exposed to chlorinated pesticides. Eur J Clin Pharmacol 5:195–198
9. Kolmodin-Hedman B (1973b) Changes in drug-metabolism and lipoproteins in workers occupationally exposed to DDT and lindane. Arch Hig Rada Toksicol 24:289–296
10. Laws ER Jr, Curley A, Biros FJ (1967) Men with intensive occupational exposure to DDT. A clinical and chemical study. Arch Environm Health 15:766–775
11. Morgan DP, Roan CC (1971) Absorption, storage and metabolic conversion of ingested DDT and DDT metabolites in man. Arch Environm Health 22:301–308
12. Morgan DP, Roan CC (1972) Loss of DDT from storage in human body fat. Nature 238: 221–223
13. Morgan DP, Roan CC (1974) Liver function in workers having high tissue stores of chlorinated hydrocarbon pesticides. Arch Environm Health 29:14–17
14. Morgan DP, Lawrence IL (1978) Blood organochlorine pesticide concentrations, clinical hematology and bio-chemistry in workers occupationally exposed to pesticides. Arch Environm Cont Toxicol 7:423–447
15. Ortelle MF (1958) Study of man with prolonged intensive occupational exposure to DDT. Arch Indust Health 18:433–440
16. Poland A, Smith D, Kuntzman R, Jacobsen M, Conney AH (1970) Effect of intensive occupational exposure to DDT on phenylbutazone and cortisol metabolism in human subjects. Clin Pharmacol Ther 11:724–732
17. Remmer H (1970) The role of the liver in drug metabolism. Am J Med 49:617–629
18. Kolmodin-Hedman B (1973a) Decreased plasma half-life of phenylbutazone in workers exposed to chlorinated pesticides. Eur J Clin Pharmacol 5:195–198
19. Thompson RPH, Stathers GM, Pilcher CWT, McLean AEM, Robinson J, Williams R (1969) Treatment of unconjugated jaundice with dicophane. Lancet 2:4
20. Wolfe HR, Armstrong JF (1971) Exposure of formulating plant workers to DDT. Arch Environm Health 23:169–176
21. World Health Organisation (WHO) Safe use of pesticides. 20th report of the WHO Expert Committee on Insecticides. WHO Technical Report Series No. 513, Geneva, Switzerland
22. Zielhuis RL (1978) Biological monitoring. Guest lecture given at the 26th Nordic Symposium on Industrial Hygiene, Helsinki, Oct., 1977. Scand J Work Environm Health 4:1–18

Received December 1, 1980 / Accepted April 1, 1981