endosulfan induced significant chromosomal changes in male rats.

The authors are grateful to Drs S. H. Zaidi and C. R. Krishna Murti for their keen interest and constant encouragement. One of the authors (GN) thanks the UGC, New Delhi for financial assistance.

**References**

1. Rowley, J. D., *J. natn. Cancer Inst.*, **52** (1974), 315.
2. Van Went-de Vries, G. F. & Kragen, M. C.T., *Fd Cosmet. Toxicol.*, **13** (1975), 177.
3. Hartwich, G., Schwanitz, G. E. & Becker, J., *Dt. Med. Wschr.*, **94** (1969), 1228.
4. Forni, A. N., Cappellini, A. P. E. & Vigliani, E. C., *Arch. Environ. Hlth.*, **23** (1971), 385.
5. Court Brown, W. M. & Doll, R., *Spec. Rep. Ser. Med Res. Coun.* **295** (1957).
6. Innes, J. R. M., Vlland, B. M., Valerio, M. G., Petrucell, L., Fishbein, L., Hart, E. R., Pallotta, A. J., Bates, R. R., Falk, H. L., Gart, J. J., Klein, G. M., Mitchell, I. & Peters, J., *J. natn. Cancer Inst.*, **42** (1969), 1101.
7. Thorpe, E. & Walker, A. I. T., *Fd. Cosmet. Toxicol.*, **11** (1973), 433.
8. Lachance, L. E., North, D. T. & Klassen, W. *in Principles of insect chemosterilization* edited by La Brecaque & Smith, C. N. (Apleton-Century Crofts, New York), 1965.
9. Cline, E., *J. Insect Physiol.*, **14** (1968), 945.
10. Grover, K. K., Pillai, M. K. K. & Dass, C. M. S., *Cytologia*, **38** (1973), 21.
11. Gaines, T. B. & Kimbrough, R. D., *Bull. Wld. Hlth Org.* **34** (1966), 317.
12. Dikshith, T. S. S. & Datta, K. K., *Bull. envirn. Contam. Toxicol.*, (1978) (in press).
13. Dean, B. J. & Thorpe, E., *Arch. Toxicol.*, **30** (1972), 39.
14. Dikshith, T. S. S. & Datta, K. K., *Bull. Environ. Contam. Toxicol.*, **9** (1973), 65.
15. Dikshith, T. S. S., *Environ. Physiol. Biochem.*, **3** (1973), 161.
16. Dikshith, T. S. S., Rockwood, W., Abraham, R. & Coulston, F., *Expl molec. Path.*, **22** (1975), 376.
17. Renecke, L. H., Klassen, W. & Norland, J. F., *Ann. Ent. Soc. Am.*, **62** (1969), 511.
18. Epstein, S. S., Arnold, E., Andrea, J., Bars, W. & Bishop, Y., *Toxocil. appl. Pharmacol.*, **23** (1970), 288.
19. Keplinger, M. L. & Deichmann W. B. *Toxicol. appl. Pharmacol.*, 7 (1965) 487.

## Effect of Oral DDT in Male Rats

V. S. N. Rao & K. S. Krishnaiah
Department of Pharmacology & Toxicology
and
P. K. Sreeraman & P. Rama Rao
Department of Pathology, College of Veterinary Science
Tirupati 517 502

*Manuscript received 2 January 1978; revised manuscript received 27 March 1978*

**Chronic treatment of mature male rats with DDT indicated induction of drug metabolizable enzymes in liver. Histological changes in testes leading to interstitial oedema, early necrotic changes in the tubules and impaired spermiogenesis were observed. No adverse effect on accessory sex organs of these animals was noticed. The changes noticed in testes in this study cannot be attributed to DDT induced enzyme induction in liver.**

In cockrels, 1, 1, 1, – trichloro - 2-bis (*p*-chlorophenyl) ethane (DDT) has been shown to produce anti-androgenic effect[1]. Its effect, however, has not been clearly demonstrated in mammals; and hence the following study was undertaken.

Twenty-four mature male colony bread albino rats (220–250 g) were divided into 3 equal groups. They were fed *ad libitum*. The rats in group II and III received DDT (50% Technical grade) as suspension in 1 ml of 1% wt/vol. of gum saline orally in daily doses of 2 and 6 mg/kg body weight respectively for a period of 8 weeks while those from group I served as controls and received gum saline only. At the end the respective groups of animals were subjected to barbiturate sleeping times by injecting pentobarbitone sodium (40 mg/kg body weight, ip). All the rats were then sacrificed, and the relative weights of liver, testes, epididymis, ventral prostate and seminal vesicles recorded. These tissues were processed for histopathology.

No toxicity signs or behavioural abnormalities were observed during the experimental period. The pentobarbital sleeping times (mean ± SD) obtained were 76.1±8.9; 31.5±7.1 and 30.2±8.9 min respectively for the groups I, II and III. They were significantly lowered ($P<0.001$) among the DDT treated as compared to controls. However there was no dose dependent decrease in the barbiturate sleeping times with a higher dose of DDT. The liver weights were considerably increased ($P<0.1$) in rats fed at 2 mg/kg only whereas the weights of testes showed an increase ($P<0.1$) in animals fed at 2 mg/kg as well as at 6 mg/kg of DDT. Testes were grossly enlarged and oedematous. Histologically, marked interstitial oedema was revealed, with no effect on spermatogenesis at the low dose of DDT. Early necrotic changes of the germinal epithelium were evident at a higher dose with impaired spermigenesis. No gross or histological changes could be observed in any other organ.

In the present investigation, a significant reduction in pentobarbital sleeping times observed in DDT treated rats indicate that the drug metabolizable enzyme induction has occurred in liver tissues. This action appears to be maximal at 2 mg/kg. as no further change was observed with a higher dose. In associattion with enzyme induction, no deleterious effect was observed in the liver either in relation to weight or histology. In this study, testes were affected both grossly and microscopically. The increase in the weights of testes observed at low dose may be due to interstitial fluid accumulation which, in turn, could lead to nectotic changes in the germinal epithelium and impaired spermiogenesis at high dose.

A marked decrease in weights of accessory sex organs of mature male rats, following chronic therapy with pentobarbital—a potent inducer of liver microsomal enzymes, was demonstrated by Levin *et al.*[2] and Fahim *et al*[3]. But in the prsent investigation it is unlikely that the observed effects on testes were due to enhanced metabolism of the endogenous androgens as DDT did not produce any adverse effect on the weights of testes and other accessory sex organs although it induced drug metabolizable enzymes in liver. Since DDT is known to influence cyclic AMP and several enzyme systems involved in carbohydrate metabolism[4], the observed effects on testes may be attributed to such an enzyme interference. Although



9248

doses of DDT employed in rats have no relevance to doses from inadvertant intake from the environment, the present study indicated the potential toxic effect of DDT on mammalian testis.


References

1. BURLINGTON, H. & LINDEMAN, V. F., *Proc. Soc. exp. Biol. Med.*, 74 (1950), 48.
2. LEVIN, W., WELCH, R. M. & CONNEY, A. H., *Steroids*, 13 (1969), 155.
3. FAHIM, M. S., DEMENT, G., HALL, D. G. & FAHIM, Z., *Am. J. Obstet. Gynecol.*, 107 (1970), 1085.
4. SINGHAL, R. L. & KACEW, S., *J. Cell Biol.*, 59 (1973), 321.


## Biochemical Changes Following Absorption of Dieldrin Through Skin


K. SOMASUNDARAM, V. N. DAMODARAN & T. A. VENKITASUBRAMANIAN*

Departments of Pathology and Biochemistry, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi 110 007


*Manuscript received* 30 *January* 1978; *revised manuscript received* 2 *May* 1978

**The toxicity of dieldrin absorbed through skin was studied by comparing the effect produced by coating various concentrations of dieldrin solution on to the skin of guineapigs. High concentrations of dieldrin increased liver RNA, protein and glycogen significantly. Ascorbic acid levels were also elevated in kidney, brain and spleen. Low concentrations of dieldrin caused no significant changes.**

DIELDRIN, a chlorinated hydrocarbon pesticide is used as a moth proofing agent on woollen garments which are constantly worn next to skin. Preliminary studies have shown no ill effects on the persons wearing these treated woollen garments for short periods of time though dieldrin is known to be absorbed cutaneously[1-5]. However, the extent of absorption and accumulation in the body and the long term cumulative effects of dieldrin are not known. The present study is on the biochemical changes induced by the percutaneous administration of dieldrin.

Chemicals and animal materials used and the treatment of animals with dieldrin have been described in detail in our previous paper[6].

After 24 hr of fasting, the animals were stunned by a blow on the head and subsequently decapitated. The liver was removed quickly, weighed and homogenized in 0.25 *M* ice-cold sucrose. Protein, RNA and glycogen were isolated as described by Shibko *et al.*[7]. DNA was isolated by the procedure of Croft and Lubran[8] and measured by Giles and Myers[9] modification of Burton's[10] method. RNA was estimated by a modified orcinol method as reported by Ceriotti[11]. Protein was assayed by the method of Lowry *et al*[2]. Glycogen was estimated by the phenol-sulphuric acid method[13].

Kidney, adrenals, spleen and half of the brain were removed, and freed of adhering blood by dipping in chilled normal saline and pressing between folds of filter paper. They were weighed quickly and homogenized in cold 10% trichloroacetic acid. Total ascorbic acid was estimated in the protein-free extracts by the method of Roe and Kuether[14].

Dieldrin treatment caused a significant increase in hepatic RNA and protein (Table 1). The concentration of DNA was not changed. These findings are in general agreement with those of Sanchez[15]. Most of the lipid soluble compounds are metabolized in hepatic cells by enzymes of endoplasmic reticulum. Organochlorine insecticides enhance the development of "smooth" membranes in the endoplasmic reticulum (SER). Extra protein is formed and simultaneously, drug metabolizing enzyme activity is increased. Dieldrin has been shown to induce a proliferation of SER in liver cells[16-18] similar to chlordane[19] A significant increase in fasting hepatic glycogen content was observed(Table 1). The glycogen content of liver at a given time represents the balance between the rates of degradation and synthesis occurring at that time. The increase in fasting hepatic glycogen content could be due to a decreased rate of glycogen breakdown (glycogenolysis) and/or an increased rate of glycogen biosynthesis (glycogenesis) in the liver of the dieldrein treated animals. Bhatia *et al.*[20] have shown that dieldrin fed rats possess a greater gycogen-synthesizing ability and lower liver phosphorylase activity than the corresponding controls. Hence the observed elevation in liver glycogen may possibly be related to inhibition of glycogen degradation coupled with an increased synthesis.

A common physiologic response to various types of acute stress is an increased secretory activity of the pituitary and adrenal glands. Since acute poisoning by organochlorine insecticides certainly represents a situation of stress, one might expect functional

TABLE 1 — EFFECT OF DERMAL ABSORPTION OF DIELDRIN ON THE MAJOR CHEMICAL CONSTITUENTS OF GUINEAPIG LIVER

[Values, expressed as mg/g wet tissue, are mean ± SE from 15 animals in each group]

| Groups | Conc. of dieldrin applied (%) | Protein | DNA | RNA | Glycogen |
|---|---|---|---|---|---|
| I | 0.0 | 221.75 ± 3.72 | 2.69 ± 0.09 | 6.21 ± 0.08 | 4.33 ± 0.22 |
| II | 0.0001 | 222.25 ± 3.27 | 2.64 ± 0.06 | 6.38 ± 0.05 | 6.56 ± 0.25† |
| III | 0.001 | 236.25 ± 2.35* | 2.68 ± 0.01 | 6.64 ± 0.19 | 6.77 ± 0.47† |
| IV | 0.002 | 233.82 ± 1.95* | 2.69 ± 0.03 | 6.53 ± 0.05* | 6.67 ± 0.30† |
| V | 0.01 | 235.40 ± 3.23* | 2.68 ± 0.02 | 6.67 ± 0.14* | 5.85 ± 0.47* |
| VI | 0.05 | 242.66 ± 2.75† | 2.74 ± 0.04 | 6.90 ± 0.09† | 6.71 ± 0.39† |
| VII | 0.1 | 241.75 ± 1.68† | 2.70 ± 0.07 | 6.77 ± 0.07† | 7.54 ± 0.31† |

*$P < 0.01$; †$P < 0.001$

*Address for future correspondence