Study of the Potential Carcinogenicity of DDT in the Syrian Golden Hamster (34740)

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The toxicity of the pesticide 1,1,1-Trichloro-2,2-bis(*p*-chlorophenyl) ethane (DDT) has been of major interest in recent years. In particular, the chronic effects of the compound have been the subject of many investigations. Since the studies reporting carcinogenicity were all, in one way or another, open to criticism (1–5), it was decided to extend carcinogenicity testing of DDT to one more species, the hamster, which has been well investigated with known carcinogens (6) of various types and which, unlike the rat, is highly susceptible to the carcinogenic action of a chlorinated hydrocarbon, carbon tetrachloride (7).

Methods. Seven- to 8-week-old Syrian Golden hamsters of both sexes were used. They were kept in plastic cages, five animals per cage, in air-conditioned rooms with artificial light. Drinking water was given *ad libitum*.

DDT (kindly provided by Geigy Agriculture Chemicals, Ardsley, New York) as 99% pure, p,p′ DDT (1,1,1-Trichloro-2-2-bis (*p*-chlorophenyl)ethane) was used.

An attempt was made to establish the LD_{50} of DDT in hamsters. DDT was dissolved in olive oil as a 6% solution and administered by stomach tube to three groups of four male hamsters each. The three groups of animals received, respectively, 450, 900, and 1800 mg/kg of body weight of DDT. As none of the animals died within 2 weeks, two additional groups, each again composed of four male hamsters, were given either 1050 or 2100 mg/kg of body weight of DDT. Hamsters receiving the highest dose showed signs of CNS irritation, such as nervousness, tremors, and convulsions, but none of them died within 2 weeks. Higher dose levels were not used due to the difficulty in obtaining a more concentrated solution of DDT in olive oil.

For purposes of comparison, the LD_{50} of the DDT used was also assessed in mice. MA inbred mice, divided into four groups of four animals for each sex, were used. The LD_{50} was established as 350 mg/kg in males and 381 mg/kg in females.

As hamsters showed resistance to the acute effects of DDT, chronic feeding experiments were started using high dose levels, namely, 500 ppm and 1000 ppm. DDT was dissolved in olive oil as a 6% solution and spread with a syringe on powdered Rockland food in glass containers, which were then put on a rolling mixer for several hours to ensure an even distribution of the oil solution. The feed was prepared every 2 weeks. The daily food consumption was between 10 and 12 g/day. This amount corresponded approximately to a daily intake of DDT of 10 to 12 mg/day in the higher dose (1000 ppm) and 5 to 6 mg/day in the lower dose (500 ppm).

Animals were divided into four experimental groups:

Group 1. Thirty females and 30 males were fed a diet containing 500 ppm of DDT.

Group 2. Thirty females and 30 males were fed a diet containing 1000 ppm of DDT.

Group 3. Twenty females and 20 males were given five doses of 0.1 ml of olive oil by stomach tube at 3-day intervals during the first 2 weeks of the experiment and received no further treatment. For the entire duration of the experiment, they were fed powdered Rockland food.

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TABLE I. Incidence of Tumors.

Group treatment	Initial no. of animals	Animals autopsied	TBA[a]	%[b]	Types of tumors; week of treatment at death in ( )	
DDT 500 ppm	30 ♀	28	4	14.2	Fibroma of uterus	(70)
					Leiomyoma of uterus	(77)
					Cortical adenoma	(84)
					Pulmonary adenomatosis	(86)
	30 ♂	30	3	10.0	Carcinoma of thyroid	(38)
					Gastric papilloma	(38)
					Reticulum cell sarcoma	(48)
1000 ppm	30 ♀	27	3	11.1	Carcinoma of adrenals	(80)
					Granuloma cell tumor of ovary	(84)
					Papilloma of stomach	(86)
	25 ♂	25	1	4.0	Hepatoma	(81)
Olive oil	20 ♀	18	1	5.5	Papilloma of forestomach	(84)
	20 ♂	19	2	10.5	Papilloma of forestomach	(80)
					Leiomyoma of stomach	(91)
Control	19 ♀	16	3	18.8	Malignant lymphoma	(62)
					Leiomyoma of uterus	(65)
					Adenocarcinoma of endometrium	(88)
	20 ♂	20	2	10.0	Pulmonary adenomatosis	(51)
					Papilloma of forestomach	(92)

[a] Tumor-bearing animals.

[b] TBA in relation to animals autopsied.

Group 4. Nineteen females and 20 males received no treatment and were fed powdered Rockland food.

Animals were weighed weekly and observed until natural death or were sacrificed when in poor condition. Autopsy was performed on all animals except a few which were missing or were too decomposed. These animals are not considered in the final results (Table I).

Histological examination was carried out on all tumors and other gross pathological lesions. Sections were stained with hematoxylin and eosin.

Results. Body weight curves are shown in Fig. 1. Animals in all groups gained weight at a similar rate for the first 3 months. As a few hamsters of the group fed 1000 ppm of DDT were losing weight and showed signs of extreme nervousness and, occasionally, convulsions, administration of DDT was suspended for 2 weeks between the 21st and the 23rd weeks of the experiment. The treatment was again stopped, for the same reason, for 2 weeks between the 39th and 41st weeks.

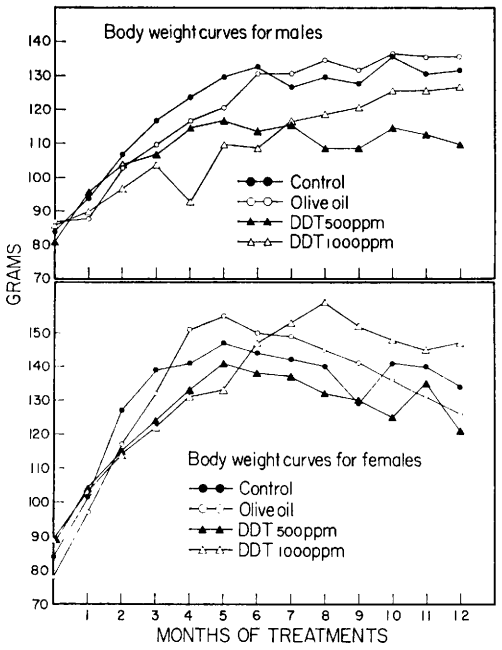

FIG. 1. Comparison of body weight by sex for four experimental groups of Syrian Golden hamsters; two of the groups receiving DDT in their diets, and two groups receiving no DDT.

Interruption of the administration of DDT for 2 weeks was, in both instances, sufficient to restore the animals to normal behavior and treatment could be resumed. The treatment was finally suspended at the 48th week of the experiment in both groups.

Incidences of tumors and survival rates are shown in Tables I and II, respectively. Incidences of tumors in DDT-treated groups did not significantly differ from those observed in the control groups. Better survival rates probably account for the slightly higher incidence of tumors in the untreated control group. At death, a considerable number of animals in all groups showed signs of acute interstitial pneumonitis, and this accounts for some early deaths. The first two tumors observed were an adenocarcinoma of the thyroid and a gastric papilloma, observed in two male hamsters of Group 1 (DDT at the 500 ppm level) which died during the 38th week of the experiment. All the other tumors were observed in animals dying later than 51 weeks after the beginning of the experiment.

Discussion. According to the literature, the LD_{50} doses of DDT given orally vary between 150 and 600 mg/kg of body weight in the rat, mouse, and cat (8). In the present study, the LD_{50} for MA inbred mice was 350 mg/kg of body weight in males and 381 mg/kg in females, which is in keeping with values reported in the literature. The LD_{50} for hamsters could not be established due to difficulty in obtaining a sufficiently concentrated solution of DDT in olive oil. Hamsters, however, were shown to survive dose levels of 2100 mg/kg of body weight. For this reason, DDT was given at the high doses of 500 and 1000 ppm.

Reports in the literature on the possible carcinogenicity of DDT in various species have revived the concern for the potential danger that this pesticide represents to man. The experimental evidence for the carcinogenicity of DDT is actually based on the induction of hepatomas in mice (9), since the data on rats and trout (2, 3) need confirmation. The present data show that the administration of DDT to hamsters at two dose levels does not result in an increased incidence of tumors, although this finding must be viewed in the light of the marked resistance of the Syrian Golden hamster to the acute effects of DDT. The different susceptibility of animal species to various chemical carcinogens is a well-known phenomenon, and the Syrian Golden hamster has recently been shown to be resistant to the carcinogenic effect of isonicotinic acid hydrazide, which, in contrast, increased the incidence of tumors in mice and rats (10, 11).

Summary. Syrian Golden hamsters survived single dose levels of 2100 mg of DDT/kg of body weight, which is about six times the LD_{50} of MA inbred mice. Long-term feeding studies in hamsters at 500 and 1000 ppm of DDT in the diet showed a slight decrease in survivals, but no significant increase of tumor incidence.

TABLE II. Survival Rates.

Group treatment	Initial no. of animals	No. of survivors at weeks of treatment										
		0	10	20	30	40	50	60	70	80	90	100
DDT 500 ppm	30 ♀	29	29	29	28	23	20	17	15	5	0	
	30 ♂	30	30	30	30	27	12	7	7	4	0	
1000 ppm	30 ♀	30	30	30	30	27	25	15	12	8	0	
	25 ♂	25	24	24	17	13	13	11	9	8	0	
Olive oil	20 ♀	20	20	19	19	18	16	15	13	6	1	0
	20 ♂	20	20	20	20	18	14	9	8	7	5	0
Control	19 ♀	19	18	18	16	16	13	8	6	4	2	0
	20 ♂	20	20	20	20	16	16	14	14	13	9	0

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