Effects of Thyroidectomy on the Storage of Organochlorine Insectisides

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Rats submitted to p,p'-DDT show morphological changes in the liver consisting of proliferation of the smooth surfaced endoplasmic reticulum and a reduction of the rough surfaced endoplasmic reticulum which is pushed toward the cell membrane (1). These features are more pronounced with increased dosage (2).

We have previously shown that the intensity of the p,p'-DDT induced changes in liver cell morphology is also increased in rats which have previously undergone thyroidectomy (3).

In order to explain these findings we decided to investigate whether thyroidectomy does not increase the amount of organochlorine insecticides in the animal body, thus exerting a more pronounced effect on the liver cell.

This paper is a report on the storage of organochlorine insecticides in the epididymal pad of normal and thyroidectomized rats when submitted to a p,p'-DDT diet, and on the biological interactions of different organochlorine insecticides in these animals.

Material and Method

Thirty-six white male rats were divided into four groups:

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Group 1 : 10 control rats

Group 2 : 6 rats thyroidectomized and autopsied three weeks afterwards.

Group 3 : 10 rats which received 200 ppm p,p'-DDT in their drinking water for 45 days.

Group 4 : 10 rats that underwent thyroidectomy under the same conditions as Group 2, and received p,p'-DDT under the same conditions as Group 3.

The animals were housed six in a cage and fed a commercial laboratory food. We used a recrystallized p,p'-DDT. This compound being insoluble in water, it was first dissolved in ethyl-alcohol (200 mg./ 6 cc.). Afterwards the alcohol was diluted in 1000 cc. of faucet water. Groups 1 and 2 also had 6% alcohol in their drinking water. Groups 2 and 4, which underwent thyroidectomy, received in addition 1% calcium lactate in their drinking water, starting with the day of the surgical intervention.

Forty-five days after the beginning of the experiment, the animals were killed under ether anaesthesia. The epididymis and its surrounding fat tissue were preserved in 10% formalin.

The organochlorine insecticides stored in the epididymal pad were analyzed by gas liquid chromatography. 500 mg. of fat tissue from the epididymal pad were ground with 20 ml. of petroleum ether. The extract was cleansed with a Kontes Co-Distiller and prepared for gas-chromato-

TABLE I

Concentration of p, p'-DDT and its Metabolites in the Epididymal Pad of the White Rate (in ppm)

Groups	Statistical Evaluation	p, p'-DDT	p, p'-DDD	p, p'-DDE	Metabolism Rate (%)
1. Control	Mean ± SD	1.66±0.36	0.31±0.04	0.66±0.20	38.4
	Range	0.75-2.17	0.26-0.40	0.36-0.95	
	P: 1 v 2	$p < 0.01$	$p > 0.10$	$p > 0.10$	
	P: 1 v 3	$p < 0.01$	$p > 0.01$	$p < 0.01$	
2. Thyroidectomy	Mean ± SD	0.66±0.22	0.31±0.08	0.63±0.16	60.3
	Range	0.47-1.06	0.16-0.38	0.46-0.88	
	P: 2 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$	
3. p, p'-DDT	Mean ± SD	170.49±50.30	16.84±3.40	33.97±22.24	24.2
	Range	78.41-261.11	12.40-21.32	12.88-75.86	
	p: 3 v 4	$p > 0.05$	$p > 0.05$	$p > 0.10$	
4. p, p'-DDT + Thyroidectomy	Mean ± SD	219.45±54.60	21.19±5.61	38.85±16.38	22.7
	Range	150.00-318.75	14.29-30.56	18.94-97.66	

graphy. A Microtek MT-220 gas-chromatograph, equipped with an electron capture detector and a strip chart recorder was used.

Results

The control rats stored 270 ppm total p, p'-DDT in the epididymal pad, of which 38.4% was metabolized to p, p'-DDD and p, p'-DDE (Table 1).

The administration of 200 ppm p, p'-DDT in the drinking water for 45 days produced an increased concentration of total p, p'-DDT in the epididymal pad of the rat up to 231.87 ppm. The storage of o, p'-DDT and of Dieldrin (occurring naturally in the body) was also increased (Table 2) while the storage of total BHC diminished from 0.089 ppm to 0.024 ppm (Table 3).

In normally fed rats thyroidectomy was associated with a significant drop in the total p, p'-DDT storage ($p < 0.01$) and a higher p, p'-DDT metabolization rate of 60.3% (as mentioned above, in the control group the p, p'-DDT metabolization rate was 38.4).

In the animals of Group 4 (thyroidectomized rats fed with p, p'-DDT) this effect is obscured by the large amount of p, p'-DDT which entered the animal body. In this group, the metabolization rate was only 22.7%.

The amount of total DDT (284.6 ppm) in this group did not differ significantly from the amount of total DDT in Group 3 (230.55 ppm).

These facts lead us to ascribe the difference in the liver cell morphology to the functional state of the thyroidectomized animals and

TABLE II

DDT and Dieldrin ppm in the Epididymal Pad of the White Rat

Groups	Statistical Evaluation	Total p,p'-DDT	Total o,p'-DDT	Total DDT	Dieldrin
1. Control	Mean ± SD	2.70±0.45	0.0286±0.0295	2.73±0.14	0.0047±0.0021
	Range	1.77-318	0.0125-0.1166	1.79-3.20	0.0030-0.0105
	p: 1 v 2	$p < 0.01$	$p > 0.10$	$p < 0.01$	$p > 0.10$
	p: 1 v 3	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
2. Thyroidectomy	Mean ± SD	1.68±0.17	0.0242±0.0064	170±0.27	0.0039±0.0019
	Range	1.42-1.91	0.0158-0.0275	1.44-1.93	0.0023-0.0073
	p: 2 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
3. p,p'-DDT	Mean ± SD	231.87±57.90	0.5931±0.1662	230.55±58.54	0.2875±0.0763
	Range	153.32-329.67	0.3391-0.7921	153.67-330.35	0.1931-0.4359
	p: 3 v 4	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.05$
p,p'-DDT + Thyroidectomy	Mean ± SD	283.93±76.10	0.6745±0.1723	284.60±76.20	0.3355±0.1176
	Range	197.30-439.51	0.4486-0.9820	197.96-440.49	0.2053-0.5425

not to the amount of DDT present in the body.

In these animals (Group 4), the storage of o,p'-DDT and Dieldrin was greater when compared with the control group ($p < 0.01$) and was also higher than in rats receiving only p,p'-DDT (Group 3).

The storage of total BHC was significantly higher (p 0.01) in the thyroidectomized rats receiving p,p'-DDT than in the non-thyroidectomized ones receiving the same amount of p,p'-DDT (Group 3).

Street & Blau (4) have shown that in rats fed on a diet containing 5 and 50 ppm DDT, the storage of Dieldrin in the fat tissue falls proportionally in the amount of DDT.

The present findings show an increased storage of Dieldrin in the fat tissue of rats receiving 200 ppm p,p'-DDT in their drinking water. This dosage represents about 4 times that used by Street and Blau since, according to our observations, rats consume an approximately equal amount of food and water. While the concentration of p,p'-DDT in the fat tissue of rats is comparable in both Street's and our study, it can be assumed that relatively high dosages of p,p'-DDT impose a higher metabolic strain which is accomplished to the detriment of the excretion of Dieldrin. This in turn, leads to an increase in its storage.

Turner, cited by Street (4) showed that Dieldrin plus DDT resulted in increased toxicity for adult milkweed bugs and found evidence of "interactions". This finding of Turner seems to support our results.

As for the way p,p'-DDT acts on the amount of Dieldrin in animal

TABLE III

B. H. C ppm in the Epididymal Pad of the White Rat

Groups	Statistical Evaluation	Total BHC (ppm)
1. Control	Mean ± SD	0.0895±0.0667
	Range	0.0449-0.2377
	p: 1 v 2	$p > 0.10$
	p: 1 v 3	$p < 0.02$
2. Thyroidectomy	Mean ± SD	0.0736±0.0164
	Range	0.0542-0.0954
	p: 2 v 4	$p > 0.10$
3. p,p'-DDT	Mean ± SD	0.0243±0.0227
	Range	0.0046-0.0752
	p: 3 v 4	$p < 0.01$
4. p,p'-DDT + Thyroidectomy	Mean ± SD	0.1240±0.0696
	Range	0.0450-0.2716

tissues as well as the role of the liver in its excretion, these are processes not yet clearly understood.

Matsumura and Wang (5) tried to provide the answer to part of these problems by an in vitro experiment. They showed that the liver tissue could be influenced by DDT "to change the absorption and desorption behaviour toward Dieldrin without involving any biochemical degradation processes against the insecticide".

Morsdorf et al. (6) showed by means of C^{14} marked Dieldrin that this insecticide is preferentially excreted in the bile after giving rise in the liver to a hydrophilic metabolite.

From this data it may be postulated that the presence of a certain amount of p,p'-DDT in the internal environment prevents Dieldrin from entering the liver cell, thus interfering with its excretion in the bile. It can be concluded that: -

a) p,p'-DDT in the diet may affect the storage level of other organochlorine insecticides depending on its concentration

b) the physiopathological state of the body has a definite influence on the biological interaction of organochlorine insecticides and on their biological effects as shown by the intensified changes in liver cell of thyroidectomized rats receiving p,p'-DDT.

Summary

Rats submitted to p,p'-DDT at 200 ppm in drinking water showed

increased p,p'-DDT storage which was not statistically different from that of thyroidectomized rats receiving p,p'-DDT. Rats receiving p,p'-DDT also showed increased fat storage of total o,p'-DDT and Dieldrin and decreased total BHC storage.

Thyroidectomy decreased the amount of p,p'-DDT naturally occurring in the animal body and raised the metabolization of this compound.

In thyroidectomized rats submitted to the same dosage of p,p'-DDT, increased storage of p,p'-DDT, o,p'-DDT and Dieldrin was found. A statistically significant increase in BHC was also observed.

It is concluded that p,p'-DDT in the diet may affect the storage level of other organochlorine insecticides depending on its concentration, and that the physiopathological state of the body, e.g. thyroidectomy has a definite influence on the storage of organochlorine insecticides in the animal body and on their biological effect.

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