Effects of Adrenalectomy on the Storage of Organochlorine Insecticides

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In addition to the factors affecting the accumulation of organochlorine insecticides in the adipose tissue such as the quantity which enters the body and age, sex and ethnic origin of the individuals studied, it has been shown that the physio-pathological state of the organism has a considerable influence on this process. Thyroidectomy (1), pregnancy (2), immunological reaction to a foreign protein (3), reduce the storage of organochlorine insecticides. Deichman found an increase in the storage of organochlorine insecticides in hypertensive subjects (4).

The presence in the animal body of certain compounds originating in the environment (xenobiotics) or occurring naturally in the body (steroid hormones) (5) accelerates the metabolism of organochlorine insecticides. This is due to the fact that organochlorine insecticides, some drugs and steroid hormones normally present in the body are substrates of the same liver oxidative enzymes and in the presence of a large amount of one substrate the activity of these unspecific enzymes which metabolize various compounds is stimulated.

Since cortisol constitutes one of the natural substrates of oxidative liver enzymes, it was decided to investigate the storage of organochlorine insecticides in adrenalectomized animals.

Material and Method

Forty-four white male rats were divided into four groups:

Group 1 - 10 control rats

Group 2 - 12 rats adrenalectomized and autopsied 3 weeks afterwards

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

Group 4 - 12 rats that underwent adrenalectomy under the same conditions as Group 2, and received p,p'DDT under the same conditions as Group 3

The animals were housed 5-6 in a cage and received water and food ad libitum. Recrystallized pure p,p'DDT was dissolved in ethyl-alcohol (200 mg/6 cc) and diluted in 1 liter faucet water. Groups 1 and 2 also had 6‰ alcohol in their drinking water. Groups 2 and 4 which underwent adrenalectomy received, in addition, 9% NaCl in their drinking water, starting on the day of the surgical operation.

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The animals were killed under ether anaesthesia. The epididymal pad was preserved in 10% formalin.

Fat tissue of the epididymal pad (500 mgs) of each rat was extracted with 20 ml petroleum ether. The extract was cleansed with a Kontes Co-Distiller. A Microtek MT-220 gas chromatograph, equipped with an electron capture detector and a strip chart recorder was used.

Results

Three adrenalectomized and 4 p,p'DDT fed, adrenalectomized rats died in the course of this experiment.

In adrenalectomized normally fed rats the amount of DDT and its metabolites stored in the epididymal pad was found to be increased. This increase was statistically significant for o,p'DDT and o,p'DDD ($p < 0.01$), p,p'DDD($p < 0.02$), p,p'DDE($p < 0.04$), total p,p'DDT($p < 0.04$) and total DDT($p < 0.06$). There was a non-significant increase of dieldrin (Tables 1, 2 and 3).

The administration of 200 ppm p,p'DDT increased the amount of p,p'DDT and its metabolites, p,p'DDD and p,p'DDE, stored in the epididymal pad of normal rats. Increased amounts of o,p'DDD and o,p'DDE which are present in the normal food were also noted. The difference between the total o,p'DDT stored in the adipose tissue of normal rats and that stored in rats fed 200 ppm p,p'DDT was significant ($p < 0.01$). The total BHC was lower in comparison with the control group ($p < 0.01$). The storage of dieldrin was significantly increased ($p < 0.01$) (Tables 1, 2 and 3).

The administration of the same amount of p,p'DDT to adrenalectomized rats was associated with an increase in the storage of p,p'DDT and its metabolites and also of dieldrin. The increase was greater than that found in normal rats receiving the same amount of p,p'DDT ($p < 0.01$). The total BHC which was decreased in normal p,p'DDT receiving rats was raised in the adipose tissue of group 4 (adrenalectomized, p,p'DDT receiving rats) to the amount found in the control group (Tables 1 and 3).

The findings reported in this paper are supportive of the existence of metabolic interactions between organochlorine insecticides, as reported previously (1).

In adrenalectomized rats there is increased storage of organochlorine insecticides, a finding which strengthens the importance of the natural substrates in inducing xenobiotic metabolizing enzymes.

Adrenalectomized rats fed high dosages of p,p'DDT store more p,p'DDT and its metabolites than normal p,p'DDT treated rats. In these rats there is also a higher storage of o,p'DDT, dieldrin and total BHC in comparison with normal rats fed at the same dosage. These findings underline the importance of the amount of natural substrates in the metabolism of xenobiotics. They suggest that great attention be paid to the patient's biochemical individuality when administering certain drugs (e.g., barbituates, anticoagu-

Table 1: Concentration of p,p'DDT and its Metabolites in the Epididymal Pad of the White Rat (in ppm)

Groups	Statistical Evaluation	p,p'DDT	p,p'DDD	p,p'DDE	Total p,p'DDT
1. Control	Range	0.7500 - 2.1666	0.2626 - 0.4000	0.3636 - 0.9464	1.7735 - 3.1790
	Mean ± SD	1.6654 ± 0.3636	0.3075 ± 0.0424	0.6581 ± 0.2000	2.7060 ± 0.4700
	1 v 2	$p > 0.10$	$p < 0.02$	$p < 0.04$	$p < 0.04$
	1 v 3	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
2. Adrenalectomy	Range	0.4544 - 5.0000	0.3888 - 10.333	0.5898 - 9.5454	3.0855 - 11.80
	Mean ± SD	2.2262 ± 1.3052	1.0797 ± 0.8184	1.2957 ± 0.7829	4.7493 ± 2.8933
	2 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
3. p,p'DDT	Range	78.41 - 261.11	12.50 - 21.43	12.88 - 75.86	153.32 - 329.67
	Mean ± SD	170.49 ± 15.93	6.86 ± 3.4284	33.97 ± 9.4974	231.87 ± 18.35
	3 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
4. p,p'DDT + Adrenalectomy	Range	166.67 - 445.00	46.66 - 116.67	48.48 - 110.60	247.49 - 684.88
	Mean ± SD	284.16 ± 87.96	71.10 ± 30.78	75.94 ± 2.0471	439.86 ± 131.19

Table 2: Concentration of p,p'DDT and its Metabolites in the Epididymal Pad of the White Rat (in ppm)

Groups	Statistical Evaluation	o,p' DDT / DDD	o,p'DDE	Total o,p'DDT
1. Control	Range	0.0069 - 0.0719	0.0050 - 0.0401	0.0128 - 0.1155
	Mean ± SD	0.0167 ± 0.0173	0.0107 ± 0.0100	0.0286 ± 0.0300
	1 v 2	$p < 0.01$	$p > 0.10$	$p > 0.10$
	1 v 3	$p < 0.05$	$p < 0.01$	$p < 0.01$
2. Adrenalectomy	Range	0.0130 - 0.0416	0.0158 - 0.0312	0.0322 - 0.0757
	Mean ± SD	0.0270 ± 0.0110	0.2300 ± 0.0057	0.0525 ± 0.0144
	2 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$
3. p,p'DDT	Range	0.0001 - 0.1718	0.2826 - 0.5568	0.3391 - 0.7921
	Mean ± SD	0.0735 ± 0.0490	0.4665 ± 0.1104	0.5931 ± 0.1661
	3 v 4	$p < 0.01$	$p > 0.10$	$p > 0.10$
4. p,p'DDT + Adrenalectomy	Range	0.0832 - 0.2692	0.2120 - 0.8214	0.2053 - 1.0540
	Mean ± SD	0.1750 ± 0.0592	0.3939 ± 0.2394	0.6237 ± 0.2828

Table 3: Concentration of Total DDT, Total BHC and Dieldrin in the Epididymal Pad of the White Rat (in ppm)

Groups	Statistical Evaluation	Total DDT	Total BHC	Dieldrin
1. Control	Range	1.7903 - 3.1967	0.0449 - 0.2377	0.0030 - 0.0105
	Mean ± SD	2.7346 ± 0.4494	0.0895 ± 0.0671	0.0047 ± 0.0021
	1 v 2	$p \leq 0.06$	$p \geq 0.10$	$p \geq 0.10$
	1 v 3	$p < 0.01$	$p < 0.02$	$p < 0.01$
2. Adrenalectomy	Range	1.5324 - 11.8475	0.0268 - 0.1517	0.0032 - 0.0406
	Mean ± SD	4.8013 ± 2.8939	0.0521 ± 0.0387	0.0126 ± 0.0112
	2 v 4	$p < 0.01$	$p \geq 0.10$	$p < 0.01$
3. p,p'DDT	Range	153.67 - 330.35	0.0046 - 0.0752	0.1931 - 0.4359
	Mean ± SD	232.47 ± 18.32	0.0242 ± 0.0224	0.2875 ± 0.0735
	3 v 4	$p < 0.01$	$p < 0.01$	$p < 0.01$
4. p,p'DDT + Adrenalectomy	Range	248.03 - 685.89	0.0247 - 0.1906	0.5150 - 1.0332
	Mean + SD	440.58 ± 131.22	0.0848 ± 0.0574	0.8018 ± 0.1910

lants).

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