PCB's and p,p′ DDE in the Blood of Cachectic Patients

by

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Many organo-halide pesticides, including dieldrin, endrin, and p,p' DDT and their metabolites, rapidly accumulate in body fat after ingestion by animals (STICKEL et al. 1969). These pesticides are excreted slowly under conditions of normal turnover of fat, but seldom reach concentrations in the blood that are high enough to be harmful to the nervous system. Experiments with birds (LUDWIG and LUDWIG 1969) and lower mammals (PAULSON 1971) suggest that the stored substances are released during the rapid metabolic mobilization of body fat that accompanies severe stress; the resulting high concentration in the blood causes serious, sometimes fatal, systemic effects. Similar effects are probably caused by polychlorinated biphenyls (PCB's--chemicals used in industry as plasticizers and dielectric materials), but investigations have only begun on their environmental toxicity. Adult female mink fed Lake Michigan coho salmon (Oncorhynchus kisutch) contaminated with PCB's failed to reproduce, and several died during a 6-month experiment (RINGER et al. 1972). When mink were fed Lake Michigan coho salmon and 30 ppm PCB's (in cereal), all died within 6 months.

The intake of relatively large amounts of DDT by humans appears to have only temporary mid-nervous-system effects, probably because the compound is rapidly absorbed from the blood by fat stores (DURHAM 1965).

In our investigation the effect of severe stress on levels of lipid-soluble organo-chlorine compounds in the venous blood was studied by the analysis of samples from nine patients hospitalized with severe wasting disease (eight had carcinomas), and a control group of 15 apparently healthy nonpatients. All were from Missouri or surrounding states.

The only organo-halides detected were p,p' DDE (a major metabolite of p,p' DDT in mammals) and PCB's. These residues in the patients' blood were apparently the result of contamination in food prior to hospitalization.

Procedure

Venous blood (10 ml) was drawn from each subject and transferred to a 15-ml graduated glass culture tube containing 100 USP units of heparin in 0.1 ml of a saline solution. The tube was

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range 2-7) and PCB's were detected only in the patients (average, 47 ppb; range 10-100).

The principal effects of organo-halide pesticides in animals are on the function of the central nervous system and on the production of liver enzymes (HAYES et al. 1956). In the present study, all of the cachetic patients were too ill to notice or complain of

TABLE Concentrations (ppb) of PCB and p,p' DDE in venous blood of cachectic patients and apparently healthy adults

Subject No.	Diagnosis	p,p'DDE (ppb)	PCB's[1] (ppb)
1	Metastatic carcinoma (died 3 days later)	10	10
2	Metastatic carcinoma (died 6 weeks later)		
	a. First blood sample	32	50
	b. Sample drawn 6 days later	38	20
3	Metastatic carcinoma (died 3 months later)	13	50
4	Myelofibrosis, pneumonia (both benign)		
	a. First blood sample	41	60
	b. Sample drawn 6 days later	19	10
5	Metastatic carcinoma (died 5 months later)	19	100
6	Metastatic carcinoma (died 4 weeks later)		
	a. First blood sample	19	100
	b. Sample drawn 6 days later	22	100
7	Metastatic carcinoma (died 9 weeks later)	12	10
8	Metastatic carcinoma	10	20
9	Metastatic carcinoma	31	30
	Patients, average[2]	21	48
	Range[2]	10-41	10-100
10-24	Nonpatients, average	3	None
	Range	2-7	detected

1/ PCB's uncorrected for recovery.
2/ Includes only first blood sample from patients 2, 4, and 6.

then sealed with a teflon-lined screw cap. After 6 days a second blood sample was taken from four of the patients--three who were in the terminal stages of carcinomatosis and one who was severely cachectic but with nonneoplastic disease. A second sample was not drawn from the remaining patients, for various medical reasons. A second sample from the nonpatients was not considered necessary because of the close agreement in the results of analyses of the first samples from this relatively large number of controls.

The blood from each subject was stored at 3 C for 1-3 days. Samples were then brought to room temperature and extracted three times with a 2 ml of redistilled hexane. The emulsion was broken by centrifuging at 4,000 g for 10 minutes. The hexane layer was drawn off with an eyedropper and dried by passing it through a 10 x 60-mm column of anhydrous Na_2SO_4. The extract was then concentrated to 2 ml in a culture tube and sealed with a teflon-lined screw cap.

The PCB's were separated from other organo-halide compounds before analysis by column chromatography (ARMOUR and BURKE 1970): 25 g of silicic acid-celite (4:1) was packed in a 22-mm I.D. column, the column was rinsed with petroleum ether, and the concentrated blood extract was put on the column with a small amount of petroleum ether and eluted with 250 ml of redistilled petroleum ether. Other organo-halide compounds were eluted with 200 ml of acetonitril-hexane-methylene chloride (1:19:80) mixture.

Samples were analyzed with a Beckman(R) gas chromatograph equipped with a nonradioactive EC detector. To help identify the compound present, we injected each sample on two columns: Column A was 0.3% OV-3 coated on 80/100 mesh Corning(R) 110 glass beads and packed in a 1.8-m x 2-mm I.D. glass column; column B was a mixture of 0.2% of Qf-1 and 0.4% DC-200 coated on 80/100 mesh Corning(R) 110 glass beads, packed in a 1.8-m x 2-mm I.D. glass column. Concentrations of DDE and PCB's were determined by comparing the peak areas of samples with those of a series of samples of known concentration. For PCB's several peaks were compared with Aroclor(R) 1254, a standard that contained most of the PCB components present in the patients' blood. No correction was made for recovery of PCB's because the blood contained several PCB compounds, each of which has many peaks that cannot be completely separated without special equipment. The recovery of DDE was 58% which agrees with other reported results (DALE et al. 1966). The use of mass spectrometry data for confirmation of the presence of PCB's was inconclusive because the sample was too small. However, several PCB chlorinated masses were observed.

Two phthalate compounds were also found in most of the blood samples but these were traced to the plastic disposable syringe used to draw the blood.

Results and Discussion

Concentrations of DDE residues in the blood were much higher in patients (21 ppb; range 10-41) than in the nonpatients (3 ppb;

previously described nervous-system symptoms such as circumoral paresthesias, malaise, skin hyper-esthesia, disturbances of equilibrium, or tremor (VELBINGER 1947a,b); all had abnormal liver function which could be attributed to their primary disease. The one death during the study (patient 1) was associated with apparent failure of all organ systems, probably because of invasion by metastatic carcinoma.

The DDE levels in the blood of cachectic patients were much lower than those in the blood of apparently healthy workers in a DDT formulating plant (LAWS et al. 1967), and in a patient given DDT therapeutically to enhance liver enzyme production (THOMPSON et al. 1969).

It would be difficult to show that the relatively low levels of DDE in the blood had any effect on the patients, even though these may not represent maximum DDE levels occurring during the illness. The PCB concentrations, however, may have been high enough to be harmful. Little is known about the toxicity of PCB's in humans, since they are used almost exclusively in industry and were not expected to appear as residues in blood.

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