

Transplacental passage of pesticides

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The present study has shown the presence of DDT and its metabolite DDE in the blood of pregnant women, fetal blood, amniotic fluid, and vernix caseosa. Transplacental passage has been clearly demonstrated by the determinations of measurable levels of DDT and DDE in cord blood, amniotic fluid, and vernix caseosa.*

THE LEVELS OF chlorinated hydrocarbon pesticides in blood and tissues of pregnant women have not been adequately studied, although it has been stated that DDT or its metabolites may be detected in most infants born in America today.^{1, 2} The occurrence of these chemicals in neonates has been documented by Denes.³ For the most part, the biological effects of acute exposure to many pesticides are well known, although this is not true regarding chronic and subacute exposure. In addition, the chlorinated hydrocarbons have been shown to be powerful stimulators of the hepatic microsomal enzyme systems and these effects remain to be determined.⁴ For this reason increased emphasis in this research area is advisable.

The application of gas chromatography and development of the electron capture detector have made possible the determination of levels of many pesticides in every tissue, thus opening new avenues of investigation. The data in this report are presented as an effort toward the clearer understanding of

the possible effects of concentrations of pesticides in blood and other tissues during pregnancy, and represent conclusive evidence of the quantitative transfer of DDT and its metabolites to the fetus. The variables of maternal race and fetal maturity are considered.

Materials and methods

All samples were collected from obstetric patients and newborn infants cared for and delivered at the Jackson Memorial Hospital in Miami, Florida. A total of 152 blood samples were obtained from 152 mothers in late pregnancy. The racial distribution was 45 Caucasians and 107 Negroes. At the time of delivery, 47 paired specimens of maternal blood and cord blood were obtained. In addition to the paired samples, cord blood was obtained from 70 newborn infants, 24 Caucasian and 46 Negro.

Whole blood samples were employed in all patients. The procedure used in the analysis of blood samples was a modification⁵ of the method described by Dale, Curley, and Cueto.⁶ Samples of heparinized blood were extracted with hexane and analyzed by a gas chromatograph using an electron capture detector. Although blood levels of several chlorinated hydrocarbon pesticides and their

From the Jackson Memorial Hospital.

**All references to DDT and DDE are to the p,p'isomers. DDT: 2,2-bis-(p-chlorophenyl)-1,1,1-trichloroethane; DDE: 2,2-bis-(p-chlorophenyl)-1,1-dichloroethylene.*

metabolites were studied, only DDT and its metabolite DDE are discussed here.

Amniotic fluid specimens from 42 women at or near term were analyzed for DDT and DDE. The amniotic fluid was collected macroscopically free of meconium and blood. After centrifugation, it was analyzed by the same method as blood.

Twelve paired samples of vernix caseosa and placenta were also collected and analyzed for DDT and DDE. Vernix caseosa was obtained by directly scraping the back and axilla of newborn infants. The selective clean-up method of Radomski and Fiserova-Bergerova,⁷ was used for the analyses of vernix caseosa and placenta.

Results

DDE levels in maternal blood, in cord blood, and amniotic fluid are shown in Table I along with statistical treatment of the data. Measurable quantities of DDE were found in all of the 152 samples from pregnant women. The levels ranged from 3 to

92 parts per billion (ppb), with a mean of 10.8 ppb in Caucasians and 15.2 ppb in Negroes. No correlation was observed between maternal age and DDE concentration, but racial differences were statistically significant.

The mean DDE level found in cord blood from 70 newborn infants was 4.8 ppb in the Caucasians and 5.9 ppb in the Negroes (Table I). When these results are arranged according to race, there is less statistical difference as compared to the maternal data. There was no statistical difference between Caucasian and Negro groups with respect to DDE levels in the 42 samples of amniotic fluid; the means for these groups were 2.4 and 2.6 ppb, respectively.

The DDT data are summarized in Table II; this includes number and percentage of samples of maternal blood, cord blood, and amniotic fluid with detectable DDT. The results in ppb from the 12 specimens of vernix caseosa, which were analyzed for DDT and DDE, are listed with the respective placental levels in Table III.

Table I. DDE levels in parts per billion in maternal blood,* umbilical cord blood, and amniotic fluid

	<i>Maternal blood</i>		<i>Cord blood</i>		<i>Amniotic fluid</i>	
	<i>Caucasian</i>	<i>Negro</i>	<i>Caucasian</i>	<i>Negro</i>	<i>Caucasian</i>	<i>Negro</i>
No.	45	107	24	46	12	30
Mean	10.8	15.2	4.8	5.9	2.4	2.6
Standard deviation	6.2	11.5	3.4	2.4	3.9	3.8
Median	9	13†	4	5‡	1	2§
Range	3 to 29	3 to 92	1 to 13	2 to 12	0 to 12	1 to 20

*At or near term.

†Significance of the difference between the medians of Caucasian and Negro values: $0.02 > p > 0.01$ by rank test.

‡Significance between medians: $0.05 > p > 0.02$.

§Significance between medians: $0.2 > p > 0.1$.

Table II. DDT levels in parts per billion in maternal blood,* umbilical cord blood, and amniotic fluid

	<i>Maternal blood</i>		<i>Cord blood</i>		<i>Amniotic fluid</i>	
	<i>Caucasian</i>	<i>Negro</i>	<i>Caucasian</i>	<i>Negro</i>	<i>Caucasian</i>	<i>Negro</i>
No.	45	107	24	46	12	30
No. with DDT†	16	71	1	4	1	1
Per cent with DDT	35.5	25.4	4.1	8.0	8.3	3.3
Maximum DDT (ppb)	17	32	5	9	6	14

*At or near term.

†DDT < 4 ppb, the lower level of sensitivity of the method to DDT.

The correlation between the levels of DDE in 47 paired maternal and fetal blood specimens, both Caucasian and Negro, is shown in Fig. 1. For Caucasian mothers and fetuses this was $r = 0.85$ ($p < 0.001$); and for Negro $r = 0.46$ ($0.01 > p > 0.001$); thus providing additional evidence of the transplacental passage of DDE.

Comment

Analysis of products of conception at 4 weeks' gestation in this laboratory has demonstrated significant levels of chlorinated hydrocarbons. In view of the relatively constant levels of DDE found in pregnant patients, it is very likely that the fertilized ovum is exposed to this substance from the beginning of its existence. Since the gonads have pesticides in them, exposure precedes zygote stage for both ovum and sperm.

Table III. DDT and DDE concentrations in parts per billion in 12 samples of paired vernix caseosa and placenta

DDT		DDE	
Vernix	Placenta	Vernix	Placenta
42.86	17.3	60.18	15.5
47.62	69.3	82.72	19.9
45.13	27.1	45.13	24.3
41.7	N.D.*	101.13	29.0
69.2	N.D.	26.7	11.0
43.8	N.D.	72.0	11.0
29.2	N.D.	40.0	22.0
84.0	N.D.	179.8	39.0
37.5	N.D.	200.0	17.0
27.1	N.D.	47.7	24.0
50.0	N.D.	106.0	31.0
50.0	N.D.	137.0	18.0

*N.D. = Not detected.

A review of the maternal DDE blood levels shows a remarkable similarity to levels in nonpregnant women described elsewhere in Dade County population surveys.⁸ This implies no change in the metabolism of these chlorinated hydrocarbons during pregnancy.

The occurrence of DDT in blood has been shown to be associated with recent exposure to DDT⁹; the levels of DDE, on the other hand, reflect chronic long-term exposure to DDT. For this reason only DDE results will be compared hereafter. Higher levels of DDE were noted in Negro patients, and the number of patients was sufficient to test the significance of this difference by statistical methods.

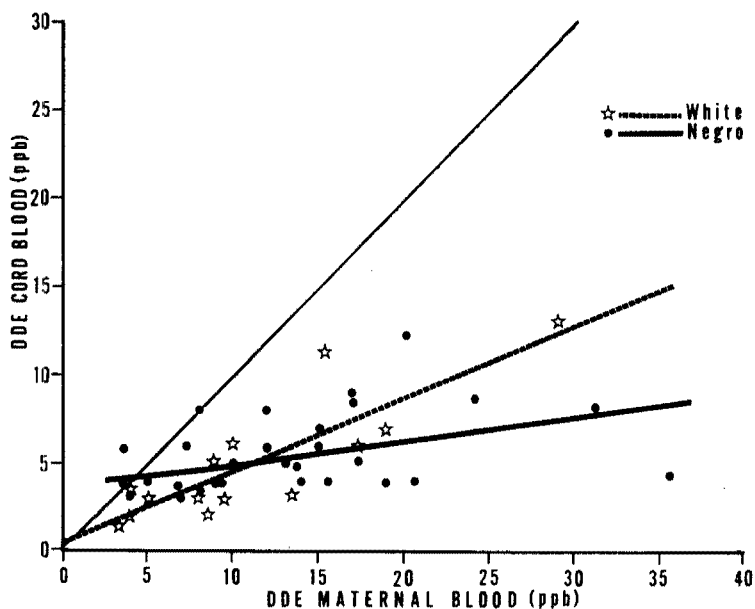


Fig. 1. Correlation of DDE in cord and maternal blood by race, in Dade County, Florida, 1968.

The cord blood levels present a distinct and interesting finding. The levels in these infants were lower than the maternal levels, but the relationship is evident from Table II. This may reflect a partial placental block, or a rapid turnover with deposition in the vernix which contained large amounts of these pesticides. Amniotic fluid values reflect maternal and fetal levels but at much lower levels and with very little statistical significance.

The findings of DDT and DDE in vernix caseosa in the high ppb range demonstrate the magnitude of these chemicals metabolized by the fetus. The most pressing problem to the obstetrician is the possible genetic and teratogenic hazard. Fahmy¹⁰ reported that a pesticide (Captan) in the embryo chick may be teratogenic. The question arises whether mutations or other effects can be produced by small exposures to chlorinated hydrocarbons as has been demonstrated with low doses of radiation. In addition, the effect of these agents on the infant's microsomal hepatic enzyme systems and resultant metabolism of other substances, and their influence on the fetus itself must be ascertained.

DDT and DDE can accumulate to high levels in the tissues without obvious effect; however, if stress arises in the fetus or mother, as frequently occurs, the fat may be metabolized rapidly and DDE then may become available in a short time and at potentially

harmful levels. The possibility that the accumulation in the fetal tissues may cause biochemical abnormalities leading to disease is under investigation. The effects upon the fetus of chronic exposure from the mother are unknown. No increase in pregnancy wastage, however, was observed in this preliminary study.

The presence of high levels of chlorinated hydrocarbons in a few premature infants at the fourth to the seventh months observed in this laboratory but not included in these data raises a number of interesting speculations. Estrogen and progesterone metabolism is greatly enhanced by the hepatic microsomal enzyme stimulation of chlorinated hydrocarbons. Hence, an elevated level could theoretically cause premature labor by decreasing the amount of available progesterone which maintains homeostasis.

The ability of DDE to aid enzyme induction has therapeutic potential. Since bilirubin metabolism is dependent upon the hepatic microsomal enzyme system, DDE could decrease the incidence of neonatal hyperbilirubinemia. Investigation in these areas is currently under way.

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