Serum DDT and DDE Levels in Pregnant Women of Chiapas, Mexico

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ABSTRACT. The authors measured the main ingredients of technical DDT (1,1,1-trichloro-2,2-bis(*p*-chlorophenyl) [p,p'-DDT]) and its principal metabolite, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene [p,p'-DDE] in serum collected from 52 pregnant women in Tapachula, Chiapas, Mexico in 1998. The median lipid-adjusted serum levels for the women were 676 ng/g p,p'-DDT (range: 56–23,169 ng/g) and 4,843 ng/g p,p'-DDE (range: 113–41,964 ng/g). In regression analysis, serum DDT and DDE increased with age (test for trend, $p = .022$) but decreased with total lactation (test for trend, $p < .001$). Residence in a house that had ever been sprayed for malaria control was also related to serum DDT and DDE. This study provides evidence of high-level exposure to DDT and DDE among pregnant women living in Chiapas, Mexico, despite countrywide restrictions on its use at the time.
<Key words: DDT, DDE, dichlorodiphenyltrichloroethane, dichlorodiphenyldichloroethylene, exposure assessment, pregnant women, serum>

DICHLORODIPHENYLTRICHLOROETHANE (technical DDT), an organochlorine pesticide, has been used to control agricultural pests and disease-bearing vectors since the 1940s.^{1,2} Because it is effective and relatively inexpensive,¹ DDT was used liberally worldwide until its negative impact on wildlife was revealed. The United States and many other countries banned its use as an insecticide in 1972.² However, DDT continues to be used in malarial endemic areas worldwide. In 1991 DDT use in Mexico was restricted to campaigns for

vector control of malaria and dengue.³ In 1995, Mexico further restricted use by initiating an integrated malarial control program that included basic hygiene, epidemiologic surveillance, and minimal pesticide use.⁴ This program led to the elimination of DDT use in Mexico in the year 2000.³

The main ingredients of technical DDT, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (p,p'-DDT) and its principal metabolite, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (p,p'-DDE) are chemically stable

and highly lipophilic, and thus persist in the environment, accumulating in the food web and in the fatty tissues of humans.^{1,2} Human exposure can be assessed by measuring p,p'-DDT and p,p'-DDE in the lipid fraction of human tissues, including serum and breast milk.⁵ DDT and its metabolites are considered to act as endocrine disruptors.^{2,6} In animal studies, *in utero* or lactational DDT exposure has been associated with alterations in reproductive and developmental outcomes, including preterm birth and reduced fetal weight,^{7,8} reduced anogenital distance and ventral prostate weight,⁹ delayed onset of puberty,¹⁰ and alterations in behavior.¹¹⁻¹⁴ Epidemiologic studies of reproductive effects of DDT in humans are limited but suggest exposure may be associated with spontaneous abortion,^{15,16} preterm birth,^{15,17,18} small-for-gestational-age births,¹⁸ longer time to conception in daughters exposed *in utero*,¹⁹ and altered reproductive function in men.²⁰

Despite the strict regulations for use of DDT in Mexico today, a number of studies of Mexican women of reproductive age indicate that they are still receiving relatively high levels of exposure to DDT based on biological measures of p,p'-DDT and p,p'-DDE levels.^{4,17,21-25} These studies suggest that, in addition to direct DDT exposure in rural areas where in-home spraying may still occur on occasion, low level indirect exposure continues throughout Mexico, most likely due to consumption of contaminated foodstuffs.^{4,17,21-25} To date, only one study has examined exposure levels in pregnant or lactating women after restrictions on DDT use were implemented, and that study was in Veracruz.^{26,27}

The purpose of this study was to determine the extent of DDT exposure among pregnant women residing in or near the town of Tapachula in Soconusco, an agricultural region located within the State of Chiapas, Mexico. In the 6-mo period prior to this study (January to June 1998) more than 500 cases of malaria were reported to the Secretariat of Health delegation of Tapachula (Dr. Juan I. Arrendondo Jimenez, Center for Malaria Research of Tapachula, personal communication). At the time of this study the National Malaria Control Program responded to reports of malaria, in part, by applying DDT indoors in all malarious areas.³ Thus, it is possible that in-home spraying of DDT for malaria control may have occurred relatively recently in the study area. In addition to measuring exposure to DDT, we aimed to determine the characteristics of pregnant women associated with an increased risk for exposure.

Method

Data collection took place at two hospitals in Tapachula. The first, Mexican Institute for Social Security (IMSS) hospital, provides care for employed families. The second, Secretariat of Health hospital,

provides care for uninsured and low-income families. This study was approved by the institutional review boards at all participating institutions including Instituto Nacional de Salud Publica, Mexico, and the University of California at Berkeley.

From July to August 1998 all pregnant women attending the prenatal clinic at either IMSS or Secretariat of Health hospital for prenatal visits were informed of the study and invited to participate. A total of 52 women (26 per hospital) agreed to participate in the study. Informed consent was obtained from all study participants. Participation included a blood draw (5–7 mL) and personal interview. The blood was collected as part of the prenatal clinical chemistry assessment; thus, no additional venipuncture was necessary.

For the interview a standardized questionnaire was administered by a trained nurse-interviewer and included information on sociodemographic characteristics, personal habits, pregnancy and lactation history, and residential history. Women were also asked questions regarding the proximity of their residence to areas where DDT may have been used, including: "Are you currently living in an area where DDT is regularly used?"; "Have you ever lived in an area where there is malaria control?"; and, "Has your house ever been sprayed as part of the malaria control program?"

When data collection was complete, serum specimens were transported to the Hazardous Materials Laboratory of the California Department of Toxic Substances Control for measurement of p,p'-DDT and p,p'-DDE by dual column gas chromatograph-electron capture detector.²⁸ Other isomeric forms of DDT and its metabolites (p,p'-DDD, o,p'-DDT, o,p'-DDE) contribute a small percentage of the total DDT^{29,30} and therefore were not measured. Levels of p,p'-DDT and p,p'-DDE were reported on a whole-weight basis as nanograms per milliliter. The average detection limit was 0.02 ng/mL of serum. Lipid-adjusted values (ng/g) were calculated by dividing p,p'-DDT and p,p'-DDE on a whole-weight basis by total serum lipid content, estimated by enzymatic determination of triglycerides and total cholesterol.³¹

For each woman, we calculated total DDT exposure as the sum of p,p'-DDT and p,p'-DDE. This value is considered a good estimate of the true total of DDT, because p,p'-DDT is the predominant form of technical DDT and p,p'-DDE is the principal metabolite.^{29,30} We also calculated the DDT/DDE ratio by dividing individual serum levels of p,p'-DDT by p,p'-DDE. In the body the half-life of DDE is longer than that of DDT; thus, the DDT/DDE ratio can help characterize the timing of the exposure. A DDT/DDE ratio greater than one may indicate recent exposure to DDT, whereas a lower DDT/DDE ratio may indicate exposure in the more distant past or perhaps ongoing indirect exposure through contaminated foodstuffs.³²

Statistical Analyses

Statistical analyses were performed using STATA 7.0.³³ Because the distributions of serum p,p'-DDT and p,p'-DDE levels were approximately log-normal, we first transformed the exposure variables using the logarithm base 10 (log). We used multiple linear regression analyses to examine the relation of serum levels of p,p'-DDT, p,p'-DDE, total DDT, and DDT/DDE ratio with covariates including age; parity; lactation; body mass index (BMI); education; residence in a house that had been sprayed as part of the malaria control program; current residence in an area with malaria control; current residence in an area of DDT use; and current residence in Tapachula. The exact age of 6 women was unknown; to include these women, we categorized age. For the final regression model we report the adjusted beta coefficients for the change in log₁₀ total DDT and nonparametric standard errors, which are valid when conventional assumptions for regressions, such as constant residual deviation, are violated.³⁴

Results

The average age of the women in this study was 24 yr and ranged from 15 to 37 yr. Forty-four percent ($n = 23$)

of the women were nulliparous. Of the 29 parous women 90% ($n = 26$) reported a history of lactation. Of these, the average length of breastfeeding reported was 20 mo, but ranged from 2 to 60 mo.

Most women ($n = 42$, 81%) were current residents of Tapachula. Many women (~20%) answered "do not know" to questions about proximity of residence to areas of regular DDT use, and as many were not familiar with DDT or other pesticides. All women, however, were able to report whether their houses had been sprayed as part of the malaria control program and 35% ($n = 18$) reported that their houses had been sprayed as part of the malaria control program. Of these, 65% ($n = 10$) reported that their houses were sprayed every year.

Levels of p,p'-DDT and p,p'-DDE were detected in all 52 samples (100%). Lipid-adjusted serum levels of p,p'-DDT, p,p'-DDE, and total DDT for the 52 women in the study are presented in Table 1 by selected characteristics. For all women, the median lipid-adjusted serum p,p'-DDT was 676 ng/g (range: 57–23,169) and median lipid-adjusted serum p,p'-DDE was 4,843 ng/g (range: 113–41,964). The median Total DDT was 6,079 ng/g, (range: 170–59,830. The median DDT/DDE ratio was 0.17 (range: 0.03–1.1).

As presented in Table 1, serum p,p'-DDT, p,p'-DDE and total DDT levels were highest among the oldest and

Table 1.—Serum p,p'-DDT, p,p'-DDE and Total DDT Levels (ng/g, Lipid-Adjusted) and DDT/DDE Ratio of Pregnant Women by Selected Characteristics, Tapachula, Mexico, 1998

Characteristic	DDT/DDE Ratio		DDT (ng/g)		DDE (ng/g)		Total DDT (ng/g)	
	<i>n</i> (%)	Median	Median	(IQR)	Median	(IQR)	Median	(IQR)
Total	52 (100)	0.17	676	(279–2,018)	4,843	(1,961–7,781)	6,079	(2,426–10,345)
Age (yr)								
15–24	30 (58)	0.18	781	(323–2,010)	5,105	(1,990–9,145)	6,115	(2,509–10,623)
25–29	16 (31)	0.15	544	(248–1,841)	4,387	(1,882–6,905)	4,950	(2,102–8,193)
30–37	6 (11)	0.24	1,165	(722–2,085)	5,762	(2,361–7,288)	7,095	(3,082–14,366)
Total lactation (mo)								
Nulliparous	23 (44)	0.15	1,124	(520–2,071)*	6,984	(4,221–13,711)*	8,282	(5,096–15,722)*
0	3 (6)	0.16	6,638	(539–12,729)	24,437	(5,630–41,964)	37,166	(6,170–48,602)
1–12	9 (17)	0.16	324	(252–1,481)	2,890	(1,915–7,726)	3,182	(2,159–9,206)
12+	17 (33)	0.22	540	(260–743)	1,934	(1,512–4,573)	2,759	(1,772–6,160)
Body mass index (kg/m ²)								
<19.8	4 (8)	0.11	306	(179–2,071)	3,507	(2,445–9,333)	3,686	(2,751–10,421)
19.8–26.0	30 (58)	0.20	595	(263–1,558)	3,061	(1,751–7,813)	3,340	(2,045–10,067)
26.1–29.0	10 (19)	0.20	2,048	(539–4,358)	6,755	(5,630–13,784)	10,773	(6,634–17,428)
>29.0	8 (15)	0.15	782	(573–1,263)	5,444	(3,467–7,355)	6,253	(4,540–8,155)
Type of hospital								
For uninsured	26 (50)	0.21	635	(244–2,010)	3,732	(1,915–6,952)	4,534	(2,160–9,206)
For insured	26 (50)	0.15	676	(361–2,071)	5,508	(3,219–9,989)	6,675	(3,470–10,623)
House ever sprayed as part of malaria control program								
No	34 (65)	0.17	544	(260–2,011)	3,963	(1,752–6,984)*	4,678	(2,160–9,206)*
Yes	18 (35)	0.19	934	(534–2,201)	6,133	(3,796–13,785)	7,605	(3,902–17,939)

Note: p,p'-DDT = DDT; p,p'-DDE = DDE; IQR = interquartile range.

*ANOVA $p < 0.05$.

the youngest women; no increasing trend with age was observed. Nulliparous and parous women who had never lactated had higher serum p,p'-DDT, p,p'-DDE and total DDT levels than women with a history of lactation. Furthermore, serum p,p'-DDT, p,p'-DDE, and total DDT levels consistently decreased with increasing length of lactation history. Women with higher BMI had higher p,p'-DDT, p,p'-DDE and total DDT levels, but not significantly. Women who reported that their house had ever been sprayed as part of the malaria control program had higher serum p,p'-DDT, p,p'-DDE, and total DDT levels than women who did not. Serum p,p'-DDT, p,p'-DDE, and total DDT levels did not vary, however, with education or current residence in the town of Tapachula (data not shown). The median DDT/DDE ratio was highest among the oldest women, women who had lactated more than 12 mo, and women attending the hospital for the uninsured, but differences were not significant.

The results of multiple linear regression analyses of serum levels of p,p'-DDT, p,p'-DDE, total DDT, and DDT/DDE ratio were similar; thus, we present only the results for total DDT. The final multivariate regression model for total DDT including age, lactation history, and in-home spraying explained 36% of the total variation observed in total DDT. In Table 2, we present the adjusted beta coefficients for a change in log total DDT levels from the final multivariate regression model. Age and lactation history were the most important predictors of total DDT levels: total DDT levels increased with age (test for trend, $p = 0.02$) and decreased with increasing length of total lactation (test for trend, $p < 0.001$). After adjusting for age and lactation history, having one's house sprayed as part of malaria control program continued to explain some of the variation in serum total DDT levels ($p = 0.14$).

Discussion

The results of this study of pregnant women residing in or near Tapachula in 1998, in the state of Chiapas, Mexico, provide evidence that exposure to p,p'-DDT and p,p'-DDE was high despite countrywide restrictions on its use at the time. The levels of p,p'-DDT and p,p'-DDE measured in serum collected from these women are higher than levels reported in serum from reproductive-age women in more urban areas such as Mexico City during the same period.^{17,23,35} In fact, the p,p'-DDT and p,p'-DDE levels reported for the women in this study exceed levels reported for women from Mexico City collected in 1989 to 1990, prior to the restriction of DDT use.⁴ The levels reported for participants in this study are in the range of those reported during the same period (1997–1998) in pregnant women in other coastal areas of Mexico,^{25–27} such as Veracruz, where direct exposure to DDT was more likely to occur than in more urban areas. In contrast, as evidence of the decreasing amount of DDT used in Mexico, the levels of p,p'-DDT and p,p'-DDE reported here are lower than those reported from rural Morelos in 1989 to 1990, before DDT use was severely restricted.⁴ Moreover, the levels reported here are roughly twice those reported from samples collected in 2003 from the same area (p,p'-DDT, median = 241 ng/g; p,p'-DDE, median = 2,695 ng/g) (Hernandez-Avila, personal communication). The serum p,p'-DDT and p,p'-DDE levels reported in this study³⁶ are on the order of those reported more than 40 yr ago in the United States (p,p'-DDT, median = 1,362 ng/g; p,p'-DDE, median = 5,119 ng/g) and are higher than those reported for Mexican-American women in the United States today (median = p,p'-DDT <10 ng/g, median = p,p'-DDE 623 ng/g).³⁷

Table 2.—Results of Multiple Regression Analysis of log₁₀ Total DDT, Tapachula, Mexico, 1998

Covariate	n	(%)	Total DDT (DDT + DDE)		
			β^*	95% CI	p
Age (yr) [†]					
15–24	30	(58)	—		
25–29	16	(31)	0.18	(–0.3, 0.7)	0.44
30–37	6	(11)	0.59	(0.1, 1.1)	0.01
Total lactation (mo) [†]					
Nulliparous	23	(44)	—		
0	3	(6)	0.26	(–0.4, 0.9)	0.44
1–12	9	(17)	–0.49	(–1.1, 0.1)	0.10
12+	17	(33)	–0.74	(–1.1, –0.3)	<0.001
House ever sprayed as part of malaria control program					
No	34	(65)	—		
Yes	18	(35)	0.19	(–0.1, 0.5)	0.14

Note: β = change in log total DDT level per unit change in covariate; CI = confidence interval.

*Adjusted for age, total lactation, and having had house sprayed for malaria control.

[†]Test for trend $p < 0.05$.

When p,p'-DDT use ceases, human exposure decreases fairly rapidly. However, exposure to p,p'-DDE, its principal metabolite, may continue because of its presence in foodstuffs. Because p,p'-DDT is steadily metabolized in the human body into mainly p,p'-DDE, the DDT/DDE ratio provides information regarding the timing of exposure to DDT.²³ Food may remain an important source of exposure despite the ban. For this study the median ratio was relatively low (~0.17), an indicator of ongoing indirect exposure such as through contaminated foodstuffs.³⁸ The median ratio observed in this study is similar to those reported for other countries where ongoing low-level DDE exposure continues to occur through contaminated foodstuffs, but lower than the DDT/DDE ratios reported for countries such as Zimbabwe and Tanzania (ratios close to 1.0), where direct exposure to DDT is still occurring because of the continued use of DDT in malaria control campaigns.³⁸ The women in this study who may have received relatively recent, direct DDT exposure (that is, those who reported having had their houses sprayed as part of the malaria control program) had a higher median DDT/DDE ratio (0.19) than those who did not (0.17). These findings suggest that women living in areas that are more likely to have in-home spraying are also more likely to consume foods highly contaminated with DDE.

Because of their long half-lives and lipophilic nature, p,p'-DDT and p,p'-DDE levels tend to increase with age³⁸ and many studies of reproductive-aged women in Mexico report a positive association of p,p'-DDT and p,p'-DDE levels with age.^{21,23,25} As with previous studies, we observed an increasing trend of total DDT with age, but it was not significant. We found that total DDT levels in this study were highest among the oldest (30–37 yr) and the youngest (15–24 yr) women. After adjusting for lactation history and in-home spraying of pesticides, we observed a positive association between age and total DDT, which suggests that younger women may have higher total DDT levels because they are less likely to have eliminated p,p'-DDT and p,p'-DDE from their bodies through lactation, but older women may have higher levels because of bioaccumulation.

Consistent with studies of Mexican women in other areas of Mexico,^{23,35,39,40} we found an inverse relation between total length of lactation and body burden of p,p'-DDT and p,p'-DDE. This suggests breastfeeding is a major pathway for elimination of p,p'-DDT and p,p'-DDE. While acting as a vehicle for elimination of p,p'-DDT from the body, breast milk also serves as a major pathway for p,p'-DDT and p,p'-DDE exposure for infants.⁴¹ Yanez et al. reported that children aged 3–14 yr from Chiapas and Oaxaca had significantly higher concentrations of p,p'-DDT in blood than adults, ages 20 to 74 yr.⁴² Because breast milk is the main source of nutrition during the first years of life for children living in these areas,⁴² the potential health consequences

as a result of lactational exposure to p,p'-DDT is of concern.

Information regarding the health effects experienced by children exposed to DDT is limited but suggests *in utero* exposure to p,p'-DDT or p,p'-DDE may affect fetal development and reproductive health later in life. A prospective study of pregnant women and their children born in the United States between 1959 and 1966 found that the likelihood of delivering preterm and, independently, the likelihood of having a small-for-gestational-age infant increased with increasing concentrations of maternal serum p,p'-DDE.¹⁸ Regarding reproductive health effects, a recent study of women born near Oakland, California, between 1960 and 1963 found an association between time to pregnancy among these women and serum p,p'-DDT levels measured among their mothers when they were pregnant with them.¹⁹

Despite the existence of strict regulations for use of DDT since 1995, this study presents evidence of continued high levels of exposure for pregnant women living near previously sprayed areas. Based on the DDT/DDE ratio, indirect exposure to DDT analogues may still be occurring through contaminated foodstuffs. In addition, breast feeding may be a major source of exposure for these women's infants and may pose a continuing health concern. As a result of the potential reproductive and developmental effects of exposure to DDT, monitoring of human exposure in areas where DDT is used should continue. Use of DDT for malaria control must be weighed against the need to contain this disease that causes more than one million deaths worldwide each year.⁴³ Until the use of effective, affordable alternatives to DDT can be implemented worldwide, the effects of exposure to DDT will remain a public health concern and should continue to be studied.

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