Effects of Residues of Organochlorine Pesticides on Reproductive Endocrinology in Pregnant Women at Delivery

Guohong Liu[1], Kedi Yang[1], Xipin Liu[2], Qifa Qin[3], Shihai Liu[1], Li Chen[4]

1. Department of Environmental Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430030, China

2. Hubei Tianmeng Hospital for Maternal and Child Care, Hubei, China

3. Xiaogan Center for Disease Control and Prevention, China

4. Hubei Family Planning Institute, China

Abstract: Some pesticides and synthetic chemicals are known to act as hormonal modulators, often possessing endocrine-disrupting effects. They are persistent and accumulative in environment, wildlife, animals and humans. The aim of our study was to explore effects of residues of organochlorine pesticides (OCPs) on reproductive endocrinology in human. We determined accumulative levels of DDT and BHC and their metabolites (isomers) in the 71 lying-in women's venous blood and documented associations among levels of total OCPs (T-OCPs), concentrations of follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol and progesterone in blood, and the expression of alpha-estrogen receptor (α-ER), beta-endorphin (β-EP) and gonadotropin releasing hormone (GnRH) mRNA in placental and umbilical cord tissues. The results showed that, a) with the increase of blood burden of T-OCPs, levels of FSH, estradiol and progesterone in the women's sera and FSH, LH and estradiol in the umbilical cord sera increased in a dose-effect manner, respectively. However, LH in the women's sera and progesterone in the cord sera presented a dose-related significant decrease ($P<0.05$); b) the abundant expression of α-ER and β-EP mRNA in the placental and cord tissues also increased in a dose-dependent manner, respectively, following the rising pesticides' burdens in maternal sera. While expression of GnRH mRNA in placental tissues presented no significant difference among the groups, moreover, its expression was not found in umbilical cord tissues; c) number of previous adverse pregnancy outcomes (PAPO) went up with the increase of the residues' burdens in maternal sera. But the number of PAPO in the high-residue group was smaller than that in the mid-residue. The average weights of newborns in the low and intermediate residue groups, but not the high residue group, were heavier than that in the control group ($P<0.05$). These findings provide evidence that the residues of OCPs in maternal blood possess endocrine-disrupting effects. It seems that estrogenic activity was dominant when concentration of T-BHC was markedly higher than that of T-DDT in blood. [Life Science Journal. 2006; 3(1): 45 - 51] (ISSN: 1097 - 8135).

Keywords: endocrine-disrupting effect; hormone; gene; organochlorine pesticides; reproductive endocrinology

1 Introduction

1, 1, 1-trichloro-2, 2-bis (p-chlorophenyl) ethane (DDT) and benzenehexachloride (BHC) of OCPs were initially introduced as an insecticide into agriculture production activities and used to control some vector-borne diseases, such as malaria and typhus (Edward, 2003). They have been officially banned in the world for two decades because of their potential harmful effects on humans, wildlife, and the environment. Their persistence, biomagnification via the food chain, reproductive toxicity, and endocrine disrupting function have been of great concerns (Matthew, 2001). Although the production and application of BHC and DDT have been officially forbidden in China since 1983, some of OCPs, for example γ-BHC, are still being produced and used in our partial regions (Yang, 2004; Bao, 1988). Numerous investigations (Yang, 2004; Bao, 1988; Yu, 2001) have reported the residues of BHC and DDT in maternal milk and their harmfulness on human health in recent decades. Their disruptive effects on reproductive endocrinology include decreased sperm counts, decreased motor ability, rising malformation ratio and

infertility, and increase of cancer incidence in testis and prostate in men and prematurity, menstrual dysfunction, hyperplasia of endometrium, habitual abortion and increase of cancer in uterus, ovary and mammary gland in women, causing great concerns in scientific community. However, the studies on the association between accumulative levels of pesticides in maternal sera and concentrations of the related hormones and expression of genes remain scarce. Tainmeng District, a residential area where the residues of DDT in the female adipose tissue samples were up to top in China in 1985 (Bao, 1988), was selected as our sampling point. In this report, we further explored effects of DDT and BHC and their metabolites on concentrations of the related hormones in maternal and cord sera and expression of genes in placental and umbilical cord tissues.

2 Materials and Methods

2.1 Subjects selection and samples collection

The pregnant women who delivered their babies at term in Tianmeng Hospital For Maternal and Child Care in Hubei province during Jan 1st to Apr 30th in 2004 were recruited for the present study, based on a) their history of potential exposure to pesticides; b) their inhabitation duration in the locality for at least five years without any known occupational exposure to DDT and BHC, and c) no hormone use for three months before their blood samples were collected.

Venous blood samples (10 ml) from the studied individuals by venipuncture at delivery as well as from the umbilical cords were collected into clear glass tubes, respectively, precipitated for 30 minutes at room temperature, and followed by centrifugation at 2 000 rpm for 5 – 10 min. Sera were then collected and stored at −20° C until analyzed. Placental tissues (10 – 15g) and umbilical cord tissue samples (10 cm) from the same subjects were also obtained, rinsed with RNase-free water, and quickly frozen in liquid nitrogen, and stored at −80° C until used for testing.

Every participant provided written informed consent and completed a questionnaire on pregnancy health. We have collected totally 71 maternal and cord blood samples and 71 placental and cord tissue samples and questionnaires, respectively. These blood and tissue samples were handled in accordance with the ethic standards established by the Committee of Ethics and Scientific Research of Tongji Medical College.

2.2 Determination of residue of OCPs in the blood from pregnant women at delivery

According to the standard method (GB/T5009.19-1996) with minimal modification, concentrations of the eight major metabolites of DDT and BHC were determined by capillary gas chromatography with electron capture detector (GC-ECD, GC 3800 chromatograph, Varian Co., USA.) using a 30 m × 0.25 mm i.d. WCOT Fused Silica CP-sil 5 CB (Varian Co., USA.) with 0.25 μm film and nitrogen carrier gas flow (99.99% purity) at 1.1 ml/min. The injector was operated in split mode, with a split ratio of 20 : 1 and injector temperature of 275℃. The oven temperature was held at 75℃ for 1 min and programmed at 20℃/min to 210℃ and held for 10 min and then programmed at 10℃/min to 260℃ and held for 10 min. Detection was by electron capture within 800 mV signal range and temperature of 300℃. Added sample volume per time was 1 μl and the minimum detectable level was 0.005 μg/L. Quantification was facilitated by comparison of peak areas with those derived from a calibration curve for each analyte. According to the concentrations of the T-OCPs in the maternal sera, the 71 studied individuals were divided into four groups, 9 of whom with non-detected level (<0.005 μg/L) were grouped as the control, other subjects whose levels of the T-OCPs were within the range of 0.005～10 μg/L, 10～40 μg/L and 40 μg/L or greater included 26, 17 and 19 individuals, respectively, of corresponding to the low, intermediate and high residue groups.

2.3 Determination of levels of the hormones in maternal and umbilical cord sera

Concentrations of FSH, LH, estradiol and progesterone in maternal and umbilical cords sera were determined using the Serozyme kits (Bio-Ekon biotechnology Co., Beijing, China), following the procedures described by the manufacturer. Concentrations of FSH and LH were determined by the technology incorporating two high affinity monoclonal antibodies into immunoenzymetric system to form a sandwich, while a high affinity monoclonal antibody was used in a competitive enzyme immunoassay system to detect levels of estradiol and progesterone. All detected values of samples, standards and controls fell within the range of quality control standard required by the kits.

2.4 Expression of α-ER, β-EP and GnRH mRNA in placental and umbilical cord tissues

According to the protocols described by Liu Hongkai and Grigorakisl SI with modification (Liu, 2004; Grigorakise, 2000), the total RNA was extracted as follows. 1 ml Trizol reagent was added into the 2 ml glass tube to homogenate tissue (50 – 100 mg). Then the lysate was moved into

1.5 ml EP tube without RNase and incubated for 5 min on ice to permit their complete dissociation. Then, 0.2 ml chloroform was added to each of the tubes, shaken for 15 sec, kept on for 2 – 3 min, and then centrifuged at 12, 000g for 15 min at 4 ℃. The colorless upper aqueous phase containing the RNA was transferred to a new tube without RNase. About 0.5 ml isopropanol was added to the tube, incubated for 2 hr at – 20 ℃, and then the RNA was precipitated by centrifugation (4℃, 10 min, 14,000 g). The RNA pellet was washed with 75% ethanol and recovered in 10 – 20 μl water treated with diethylene pyrocarbonate (DEPC). The RNA purity was checked by both gel electrophoresis and optical density ratio, which was between 1.8 and 2.0. The RNA solution was preserved at – 70℃ for further analysis.

3.0 μg of total RNA from each sample was reverse transcribed into cDNA using a reverse transcription kit (Fermentas Life Sciences Co., USA) in 12 μl of reaction mixture containing oligo dT primer and MMLV reverse transcriptase at 42℃ for 1 hour. This reaction was stopped by incubation at 94 ℃ for 5 min. Aliquot of 1 μl of the reverse transcription reaction was amplified with Taq polymerase (Fermentas Life Sciences Co., USA) in a final volume of 50 μl containing 25 mM $MgCl_2$, 20 pmol of sequence-specific primers for α-ER, β-EP and GnRH (all primers were synthesized by Bioasia corporation in Shanghai, China) and 2mM dNTP Mix. The mixture was amplified by PCR for 35 cycles for α-ER (1 cycle = 94 ℃ for 50 sec, 57 ℃ for 45 sec, and 72 ℃ for 1 min), or 35 cycles for β-EP (1 cycle = 94 ℃ for 45 sec, 55 ℃ for 45 sec, and 72 ℃ for 2 min), or 35 cycles for GnRH (1 cycle = 94 ℃ for 50 sec, 60°C for 45 sec, and 72 ℃ for 2 min). Primer sequences were designed as follows. α-ER: 5′-GGC TAC ATC ATC TCG GTT CC-3′ and 5′-GTG ATC TTG GCC AGG ACT CG-3′ (product length was 369 bps). β-EP: 5′-CCT ACA GGA TGG AGC ACT TC-3′ and 5′-GTA GGC GTT CTT GAT GAT GG-3′ (product length was 130 bps). GnRH: 5′-AGC CAG CAA GTG TCT CTG AG-3′ and 5′-TTC CAC GCA CGA AGT CAG TA-3′ (product length was 224 bps). Products of the PCR reaction (5 – 10 μl) were analyzed on 2% agarose gels in 0.5 × TBE, stained with ethidium bromide (EB), and photographed. To correct the amount of RNA analyzed and to evaluate the relative levels of α-ER, β-EP, and GnRH expression, a ubiquitin gene (β-actin) was also used as the internal control. The relative expression was determined by using the ratio of intensity of target genes to that of β-actin.

2.5 Statistical analysis

The analysis of variance (ANOVA) with SNK test was used to compare the data. If their distribution deviated from normality or presented heterogeneous variances, nonparametric methods (Wilcoxon test) were used instead, and the statistics were expressed as median/inter quartile range. A difference at $P<0.05$ was considered statistically significant.

3 Results

3.1 Comparison of major characteristics for the studied mothers and their babies and families in various groups

The studied pregnant women's age range was from 21 to 35 yr and there was no significant difference among the four groups. The indexes such as average pregnant times, average laboring times, average pregnant duration, percent of vaginal delivery (VD) and elective cesarian section (CS), percent of single-fetus term delivery and average monthly family income among the groups presented also no significance ($P > 0.05$). However, the number of PAPO (i.e., spontaneous abortion, induced abortion, ectopic pregnancy, premature delivery, post-term delivery, et al.) in the low, intermediate, high residue groups were greater than that in the control group and significant differences were found. Average weights of newborns in low and intermediate groups were markedly heavier than that in the control group, and the differences among groups were statistically significant ($P < 0.01$). Nevertheless, no difference was observed between high residue group and the control group ($P > 0.05$). It was interesting that rank of the weight from high to low was the low > intermediate > high residue > the control groups (Table 1).

3.2 Levels of major metabolites of DDT and BHC in blood from pregnant women at delivery

The eight isomers, α-, β-, γ-, δ-BHC and p, p′-DDE, o, p-DDT, p, p′-DDD, p, p′-DDT, were found in the 62 individuals but not the 9 samples in the control group, where concentrations of residues in maternal sera were lower than the minimum detectable level (MDL). In the low, intermediate and high residue groups, the percentages of α-BHC (50.00%, 52.94% and 63.16%) and o, p-DDT (11.54%, 41.18% and 78.95%) determined in the blood were relatively higher in comparison with those of β-BHC (23.08%, 47.06% and 36.84%) and p, p′-DDE (19.23%, 35.29% and 42.11%). In the low, intermediate and high residue groups means of the total BHC, the sum of α-, β-, γ- and δ-BHC, were 4.65 μg/L, 15.09 μg/L and

56.49 μg/L, and means of the total DDT which equaled to the sum of p,p′-DDE, o,p-DDT, p,p′-DDD and p,p′-DDT were 0.72 μg/L, 9.12 μg/L and 54.56 μg/L, respectively. The former were significantly higher than the latter. In the control, low, intermediate and high residue groups the means of T-OCPs, sum of the eight isomers, were < 0.005 μg/L, 5.37 μg/L, 24.21 μg/L and 111.05 μg/L, respectively. Significant differences were found ($P<0.05$) (Table 2).

Table 1. Comparison of major characteristics for the studied mothers and their babies and families in various groups

Parameter	Groups			
	Control($n=9$)	Low($n=26$)	Intermediate($n=17$)	High($n=19$)
Mother's age (years)	26.56±3.61	25.88±3.18	26.82±3.88	25.79±3.49
Average pregnancy number	1.67±1.12	1.73±1.08	2.18±1.01	2.32±1.57
Average delivery number	1.22±0.44	1.19±0.40	1.24±0.44	1.42±0.84
Average pregnancy weeks	38.7±4.12	38.5±3.66	38.2±4.51	38.1±4.22
Average number of PAPO	0.33±0.50	0.42±0.50[a]	0.59±0.51[ab]	0.53±0.51[abc]
Percent of VD(%)	33.33	11.54	11.76	21.05
Percent of CS(%)	66.67	88.46	88.24	78.95
Percent of single-fetus term delivery(%)	100	96.15	100	100
Average weight of newborn(g)	3228±404.75	3408±319.28[a]	3353±379.75[ab]	3250±463.98[bc]
Average monthly family income(yuan)	1844.4±127.5	1830.8±201.3	1788.2±154.3	1705.3±142.5

Note. Data in the table are mean±SD except percentage. [a]Values compared to the control, $P<0.05$. [b]Values compared to the low-residue group, $P<0.05$. [c]Values compared to the intermediate, $P<0.05$.

Table 2. Levels of metabolites of DDT and BHC in maternal blood

Parameter	Groups			
	Control($n=9$)	Low($n=26$)	Intermediate($n=17$)	High($n=19$)
Percent of detected α-BHC (%)	<MDL	50.00	52.94	63.16
Percent of detected β-BHC (%)	<MDL	23.08	47.06	36.84
Percent of detected γ-BHC (%)	<MDL	3.85	29.41	68.42
Percent of detected δ-BHC (%)	<MDL	42.31	35.29	5.26
Percent of detected p,p'-DDE (%)	<MDL	19.23	35.29	42.11
Percent of detected o,p'-DDT (%)	<MDL	11.54	41.18	78.95
Percent of detected p,p'-DDD (%)	<MDL	0.00	11.76	31.58
Percent of detected p,p'-DDT (%)	<MDL	3.85	0.00	21.05
Total BHC(μg/L) ($\bar{\chi}\pm S$)	<MDL	4.65±2.42[a]	15.09±9.25[ab]	56.49±38.74[abc]
Total DDT(μg/L)($\bar{\chi}\pm S$)	<MDL	0.72±1.65[a]	9.12±8.56[ab]	54.56±55.43[abc]
T-OCPs (μg/L)($\bar{\chi}\pm S$)	<MDL	5.37±2.22[a]	24.21±9.75[ab]	111.05±45.26[abc]

Note. All targeted components were not determined in the samples of the control group. MDL: minimum detectable level. [a]Values compared to the control, $P<0.01$. [b]Values compared to the low-residue group, $P<0.01$. [c]Values compared to the intermediate, $P<0.05$.

3.3 Concentrations of FSH, LH, estradiol and progesterone in maternal and cord sera

As shown in Table 3, with the increase of blood burden of T-OCPs, levels of FSH, estradiol and progesterone in the maternal sera and FSH, LH, and estradiol in the umbilical cord sera increased, respectively. There was an obvious dose-effect relationship. However, LH in the women and progesterone in the cord sera decreased in a dose-dependent manner, respectively, as accompaniment with the rising pesticides' levels. Significance was found between groups ($P<0.05$).

3.4 Expression of α-ER, β-EP and GnRH mRNA in placental and cord tissues

Table 4 indicates that abundant expression of α-ER and β-EP in the placental and cord tissues went up respectively following the rising pesticides' burdens in maternal sera. Their dose-effect relationship existed steadily ($P<0.01$). Expression of GnRH mRNA in placental tissues did not show statistically significant difference ($P>0.05$), although levels of various residue groups were higher as compared to the control group. It was noticed that transcription of GnRH gene in cords was not detected in the present study.

Table 3. Comparison of levels of FSH, LH, estrodial and progesterone in sera of women and cord($\bar{\chi} \pm S$)

Parameter		Groups			
		Control($n=9$)	Low($n=26$)	Intermediate($n=17$)	High($n=19$)
Maternal sera	FSH (mIU/ml)	0.83 ± 0.29	1.08 ± 0.48	1.63 ± 0.31^{ab}	2.27 ± 0.61^{abc}
	LH (mIU/ml)	1.47 ± 0.45	1.08 ± 0.53	0.80 ± 0.36^{a}	0.63 ± 0.21^{ab}
	estrodial (ng/ml)	41.80 ± 7.72	52.82 ± 7.52^{a}	54.99 ± 8.30^{a}	43.15 ± 8.25^{bc}
	progesterone (ng/ml)	$264:04 \pm 29.21$	294.59 ± 16.50^{a}	306.94 ± 22.61^{ab}	327.22 ± 31.38^{abc}
Cord sera	FSH (mIU/ml)	1.41 ± 0.41	1.54 ± 0.50	1.62 ± 0.56	2.91 ± 0.91^{abc}
	LH (mIU/ml)	0.60 ± 0.28	0.64 ± 0.38	0.79 ± 0.29	2.07 ± 0.81^{abc}
	estrodial (ng/ml)	12.53 ± 3.28	18.01 ± 7.01^{a}	24.03 ± 3.92^{ab}	23.83 ± 9.98^{ab}
	progesterone (ng/ml)	804.47 ± 73.76	767.04 ± 62.32	654.74 ± 24.45^{ab}	604.70 ± 26.82^{abc}

Note. [a]Values compared to the control, $P<0.01$. [b]Values compared to the low-residue group, $P<0.01$. [c]Values compared to the intermediate, $P<0.05$.

Table 4. Comparison of abundant expression of α-ER, β-EP and GnRH mRNA in placental and cord tissues($\bar{\chi} \pm S$)

Gene mRNA		Groups			
		Control($n=9$)	Low($n=26$)	Intermediate($n=17$)	High($n=19$)
Placental tissues	α-ER	1.62 ± 0.41	1.93 ± 0.76	2.13 ± 1.00	2.42 ± 0.92^{a}
	β-EP	0.36 ± 0.17	0.50 ± 0.17^{a}	0.62 ± 0.22^{a}	0.68 ± 0.25^{ab}
	GnRH	1.61 ± 0.68	1.80 ± 0.54	2.09 ± 0.63	1.68 ± 0.56
Umbilical cord tissues	α-ER	1.49 ± 0.45	1.72 ± 0.68	1.90 ± 0.91	2.14 ± 0.82^{a}
	β-EP	0.24 ± 0.17	0.31 ± 0.14	0.43 ± 0.19^{ab}	0.46 ± 0.18^{ab}

Note. [a]Values compared to the control, $P<0.01$. [b]Values compared to the low-residue group, $P<0.01$. [c]Values compared to the intermediate, $P<0.05$.

Data in the table were the ratio of densitometric units of targeted genes to β-actin.

3.5 Rank correlation between the expressional abundance of the genes in placental and umbilical cord tissues and levels of the hormones in maternal and cord sera

As shown in Table 5, significant correlations were found among the following indexes such as, a) between expressional abundance of β-EP in placental and cord tissues and concentrations of FSH in maternal and cord sera ($r=0.2963, P=0.0121$; $r=0.3053, P=0.0096$; $r=0.2793, P=0.0183$; $r=0.2354, P=0.0482$), respectively. b) between expression of β-EP in cord tissues and level of progesterone in maternal blood ($r=0.2744, P=0.0206$). c) between concentration of estradiol in cord sera and expression of α-ER and β-EP in placental and cord tissues ($r=0.4732, P\leqslant 0.0001$; $r=0.4700, P\leqslant 0.0001$; $r=0.5633, P\leqslant 0.0001$; $r=0.5243, P\leqslant 0.0001$), respectively. d) between level of progesterone in cord sera and expression of α-ER and β-EP in placental and cord tissues ($r=-0.2584, P=0.0296$; $r=-0.2425, P=0.0416$; $r=-0.4303, P=0.0002$; $r=-0.4016, P=0.0005$), respectively.

Table 5. Rank correlation between the expressional abundance of α-ER, β-EP and GnRH in placental and cord tissues and the levels of FSH, LH, estradiol and progesterone in maternal and cord sera

Parameter		Placental tissues			Umbilical cord tissues	
		α-ER	β-EP	GnRH	α-ER	β-EP
Maternal sera	FSH	$r=0.2329$ $P=0.0506$	$r=0.2963$ $P=0.0121$	$r=0.1295$ $P=0.2818$	$r=0.2162$ $P=0.0702$	$r=0.3053$ $P=0.0096$
	LH	$r=0.0874$ $P=0.4688$	$r=-0.1474$ $P=0.2201$	$r=-0.1660$ $P=0.1666$	$r=0.0756$ $P=0.5308$	$r=-0.0923$ $P=0.4439$
	estradiol	$r=0.0069$ $P=0.9545$	$r=-0.0528$ $P=0.6617$	$r=0.0432$ $P=0.7208$	$r=0.0310$ $P=0.7976$	$r=-0.0233$ $P=0.8469$
	progesterone	$r=0.1772$ $P=0.1392$	$r=0.2251$ $P=0.0591$	$r=-0.0419$ $P=0.7286$	$r=0.1604$ $P=0.1815$	$r=0.2744$ $P=0.0206$
Umbilical cord sera	FSH	$r=0.1927$ $P=0.1073$	$r=0.2793$ $P=0.0183$	$r=0.0048$ $P=0.9683$	$r=0.1812$ $P=0.1305$	$r=0.2354$ $P=0.0482$
	LH	$r=-0.0044$ $P=0.9708$	$r=0.2142$ $P=0.0729$	$r=0.1396$ $P=0.2457$	$r=-0.0195$ $P=0.8715$	$r=0.1663$ $P=0.1658$
	estradiol	$r=0.4732$ $P=<0.0001$	$r=0.5633$ $P=<0.0001$	$r=-0.0844$ $P=0.4841$	$r=0.4700$ $P=<0.0001$	$r=0.5243$ $P=<0.0001$
	progesterone	$r=-0.2584$ $P=0.0296$	$r=-0.4303$ $P=0.0002$	$r=-0.0767$ $P=0.5250$	$r=-0.2425$ $P=0.0416$	$r=-0.4016$ $P=0.0005$

4 Discussion

Although OCPs (i.e., DDT and BHC) have been officially banned for decades in the world, their chemical characteristics predict that once into the food chain these pesticides are difficult to eliminate. Moreover, as a consequence of their global distillation effect, high lipophilicity and long persistence, they may have multi harmful effects on humans, animal, wildlife and environment. These ubiquitous organochlorine pollutants have shown toxicity, mutagenesis, carcinogenesis, and especially endocrine disrupting function, which have aroused increasing concerns (Yu, 2001; Fernando, 2001; Chou, 2004). However, some of OCPs are still produced and used due to a type of cheap and broad-spectrum insecticide in some regions in China (Chou, 2004). Therefore, high level of residues of BHC and DDT are still found in part of food, milk and blood, etc. The studies on their harmful effects on human and animals, especially endocrine-disrupting effects, are necessary and significant. In present study Tianmeng district, as a cotton-planting region where DDT and BHC were used extensively and massively during the last century, was selected as our sampling point. Its aim is to understand effects of residues of OCPs on reproductive endocrine function in the population who have inhabited such a heavily polluted area by DDT and BHC for five years or more.

71 lying-in women were recruited to participate in this study. Our results indicated that high levels of residues of OCPs were still capable to be found in part of the subjects. The 19 individuals of high residue group possessed means of the T-BHC, T-DDT and T-OCPs of 56.49, 54.56, 111.05 μg/L, corresponding to medians of 50.00, 41.80, 98.70 μg/L, respectively. This was markedly higher than that in its adjacent district-Xiaogan where means of T-DDT and T-BHC of the sampled people were 3.61 ± 0.22 μg/L, 5.96 ± 0.41 μg/L, respectively (Liu, 2004).

The hypothalamic-pituitary-ovarian axis is an integrated and coordinated neuroendocrine system which regulates female reproductive endocrine activity. GnRH secreted in pulse by hypothalamic stimulates release of FSH and LH synthesized by pituitary, which regulates synthesis and secretion of estradiol and progesterone. At the same time, estradiol and progesterone regulate in feedback synthesis and secretion of GnRH, FSH, and LH. Beta-endorphin, as a neuropeptide, mostly suppresses activity of GnRH. Estradiol binding to its receptor regulates transcription and translation of the target genes. Therefore, to some extent, changes of quantity and activity of estradiol and ER indicate estrogenic and anti-estrogenic activity for xenobiotics (Antonin, 2003; Graeme, 2002). Changes of concentrations of hormones in blood and expressional abundance of some genes in placental and umbilical cord tissues are probably a sensitive biomarker, which indicates that some xeno-compounds are able to disrupt endocrine function. The present study revealed that not only concentrations of FSH, LH, estradiol and progesterone but also abundant expression of α-ER, β-EP and GnRH mRNA could be changed, which corresponded to blood burden of metabolites of DDT and BHC in maternal sera. Moreover, number of PAPO increased due to residues of OCPs. All these show that residues of DDT and BHC possess endocrine-disrupting effects. It seems that estrogenic activity was dominant when concentration of T-BHC was markedly higher than that of T-DDT in maternal blood (Deborah, 2002).

In conclusion, concentrations of residues of OCPs are still relatively high in some people of China. They are capable to disrupt endocrine function so as to induce reproductive dysfunction and developmental malformation. However, many problems have been not still solved. Therefore, further studies are needed to address effects of exposure to xenoestrogens during a specific period of development, probable roles of other substances with proven or suspected hormonal activity, potential synergism of such compounds, and differences in individual susceptibility.

Acknowledgments

We are grateful to the staff members at the Tianmeng Hospital for Maternal and Child Care for their assistance during samples collection. The authors would like to express their sincere thanks to Dr. Wei Qingyi for his critical review of the manuscript.

Correspondence to:
Kedi Yang
Hubei Tianmeng Hospital for Maternal and Child Care
Wuhan, Hubei 430030, China

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Received November 5, 2005