BODY BURDEN OF DIOXINS AND ESTROGEN DEPENDENT DISEASES

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Abstract
We aimed to examine the association between increased serum dioxins concentration and estrogen dependent disease, including endometriosis, adenomyosis, and leiomyoma. Cases were from Department of Obstetrics and Gynecology using laparoscopy for diagnosis of the 3 diseases in southern Medical center during January, 2005 and December, 2006. Controls were from either the same department or health check unit and free from the above three diseases, matched for age, body mass index (BMI), and cigarette smoking status. Serum levels of polychlorinated dibenzo-p-dioxins (PCDDs), dibenzo-furans (PCDFs), and polychlorinated biphenyls (PCBs) were quantified by high resolution (HR) gas chromatography and HR mass spectrometry. The current report was based on 72 subjects aged 25~45 years (26 cases and 46 controls） with dioxins and PCBs all measured. Total PCDFs, PCDDs and PCBs are significantly higher in cases (6.63 pg-TEQ/g lipid, 8.07, and 8.17 respectively) than in controls (4.58, 6.62, 5.82; *p* value= 0.001, 0.027, 0.010 respectively). The increased risk remained after adjustment for age, BMI, parity, and breast-feeding by logistic regression. There is a clearly positive association between Dioxins/PCBs body burden and the estrogen dependent disease even with small sample size, The effect is worth of noting and investigation of mechanisms is warrant

Introduction
Previous studies showed dioxins are well established endocrine disrupters[1]. Exposure to dioxins will cause alteration of estrogen metabolism in women of reproductive age[2-5]. We aimed to know the increased serum dioxins concentration with estrogen dependent disease, such as endometriosis, adenomyosis, and leiomyoma.

Materials and Methods
This is a matched case control study of participants recruited in southern Medical center during January, 2005 and December, 2006 from southern Taiwan. Cases were from Department of Obstetrics and Gynecology using laparoscopy for diagnosis of endometriosis, adenomyosis and leiomyoma. Controls were from either the same department or health check unit and free from the above three diseases. Serum levels of polychlorinated dibenzo-p-dioxins (PCDDs), dibenzo-furans (PCDFs), and polychlorinated biphenyls (PCBs) were quantified by high resolution (HR) gas chromatography and HR mass spectrometry. The current report was based on 72 subjects aged 25~45 years (26 cases and 46 controls） with dioxins and PCBs all measured.

Results and Discussion
The main general characteristics are not different between cases and controls (Table 1), Total PCDFs, PCDDs and PCBs are significantly higher in cases (6.63 pg-TEQ/g lipid, 8.07, and 8.17 respectively) than in controls (4.58, 6.62, 5.82; *p* value= 0.001, 0.027, 0.010 respectively), Total PCDDs/DFs and Total Dioxins/PCBs the results are the same (*p* value = 0.002, 0.010, Figure 1), the levels in women with leiomyoma are significantly higher than in controls (Figure 2). The disease risk and increased levels of PCDF (Odd Ratio=1.63, 95%CI=1.11-2.40), Total Dioxins/PCBs (OR=5.84, 95%CI=1.42-23.98) after adjustment for age, BMI, parity, and breast-feeding by logistic regression (Table 2). In correlation analysis, Insulin is significantly negative relation on Total PCDFs, Total PCDDs/DFs, Total PCBs and Total Dioxins/PCBs (*p*= 0.004, 0.035, 0.034, 0.018), negative relation between leptin and Total PCDFs (*p* =0.023) (Table 3). In the cases AFP is significant positive correlation on Total PCBs and Total Dioxins/PCB (*p* = 0.003, 0.020) and Leptin is negative correlation on Total PCDFs and Total PCDDs/DFs (*p* =0.018, 0.016) (Table 4).

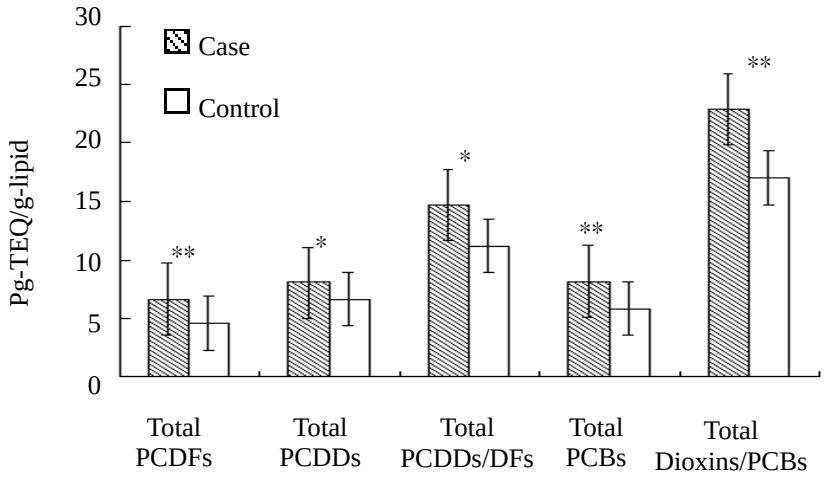
There is a clearly positive association between Dioxins/PCBs body burden and the estrogen dependent disease even with small sample size, The effect is worth of noting and investigation of mechanisms is warrant

Table1: General characteristics of cases and their controls

	Case n =26	Control n =46	*p*-value
Age (mean, SD)	34.04 ± 6.11	31.00 ± 7.26	0.270[a]
BMI (mean, SD)	22.30 ± 4.30	24.00 ± 3.63	0.053[a]
Age at menstrual (mean, SD)	12.00 ± 1.53	13.47 ± 1.29	0.072[a]
Menstrual cycle (days, SD)	28.19 ± 3.56	29.97 ± 4.30	0.080[a]
Menstruate (days, SD)	5.98 ± 2.41	5.52 ± 1.30	0.444[a]
Parity (%)			
0	16 (61.5)	23 (51.1)	
>1	10 (38.5)	22 (48.9)	0.463[b]
Breast feeding (%)			
Ever (≧ 1 parity)	3 (11.5)	9 (20.0)	0.051[b]
Passive smoke (%)			
Husband	7 (26.9)	10 (23.3)	
Public	9 (34.6)	7 (16.3)	0.141[b]
None	10 (38.5)	26 (60.5)	
Alcohol (%)			
Yes*	6 (24.0)	5 (11.1)	0.205[b]

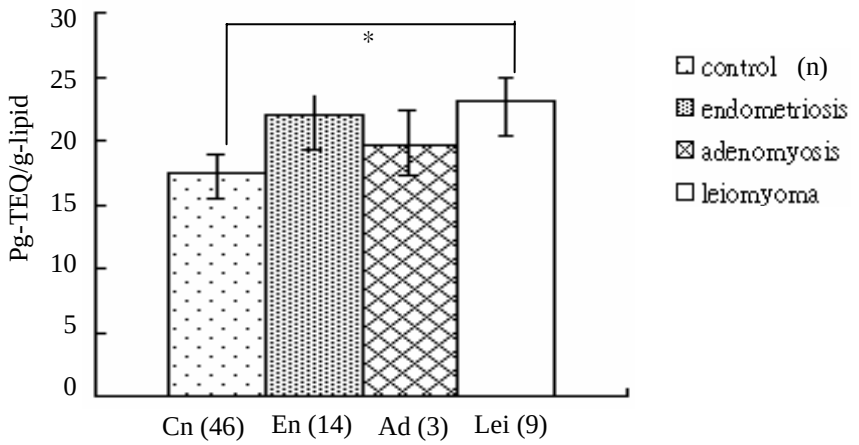
p-value: [a] Student T-test, [b] Fisher`s exact
*: ≧ Frequency of alcohol: 1 / week regularly

Figure 1: The Dioxins and PCBs level in case and their control



p –value: *<0.05, **<0.01, the error bar shows Standard Error of means

Figure 2: The distribution pattern of Total Dioxins/PCBs among cases and controls



p -value: * <0.05, Error bar shows 95% Confidence Interval of means

Table 2: Odds ratio for above medium levels of dioxins and PCBs by Logistic regression analysis

	Case n (%)	Control n (%)	OR (95%CI)	*p*-value
Total PCDFs[a]				
≦5.00	5 (19.2)	31 (67.4)	1	0.012
＞5.00	21(80.8)	15 (32.6)	1.63 (1.11-2.40)	
Total PCDDs[a]				
≦7.00	8 (30.8)	30 (65.2)	1	0.105
＞7.00	18 (69.2)	16 (34.8)	3.21(0.78-13.18)	
Total PCBs[a]				
≦6.00	11 (42.3)	26 (56.5)	1	0.268
＞6.00	15 (57.7)	20 (43.5)	2.12 (0.56-8.07)	
Total PCDDs/DFs[a]				
≦12.00	6(23.1)	29 (63.0)	1	0.074
＞12.00	20 (76.9)	17(37.0)	3.79(0.56-16.34)	
Total Dioxins/PCBs[a]				
≦18.00	7(26.9)	29 (63.0)	1	0.014
＞18.00	19(73.1)	17(37.0)	5.84 (1.42-23.98)	

a: Adjust for age, BMI, breast-feeding and parity.
Unit: pg-TEQ / g-lipid

Table 3: Correlation between cancer marker, hormone and Total Dioxins and PCBs

	Total PCDFs	Total PCDDs	Total PCDDs/DFs	Total PCBs	Total Dioxins/PCBs
CA125	0.040	0.007	0.007	-0.123	-0.040
AFP	0.081	0.259	0.213	0.211	0.213
CEA	0.060	0.199	0.178	0.114	0.154
Insulin	-0.387*	-0.228	-0.287*	-0.290*	-0.322*
Leptin	-0.314*	-0.179	-0.253	-0.261	-0.255
Adiponetin	-0.067	-0.014	-0.027	-0.050	-0.076
IGF1	-0.268	-0.226	-0.247	-0.231	-0.277
Testosteron	-0.116	0.085	0.014	-0.012	-0.017
Prolactin	0.157	-0.104	-0.021	0.008	0.016

Abbreviation: AFP, α-fetal protein; CEA, Carcinoembryonic antigen
*: p –value < 0.05
All cancer marker and hormone values are geometric mean

Table 4: AFP and Leptin for cases and controls in relation to Total Dioxins and PCBs

		Total PCDFs	Total PCDDs	Total (PCDFs/PCDDs)	Total PCBs	Total Dioxins/PCBs
Control	AFP	0.005	0.314	0.154	-0.105	0.122
	Leptin	-0.064	-0.015	-0.038	-0.176	-0.034
Case	AFP	0.353	0.283	0.352	0.507*	0.457*
	Leptin	-0.497*	-0.306	-0.429*	-0.305	-0.358

*: p –value < 0.05

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