# PERSISTENT ORGANIC POLLUTANTS IN ADIPOSE TISSUES OF PATIENTS WITH UTERINE LEIOMYOMA

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## Introduction

Hong Kong, located in southeast China, is one of the most densely populated cities in the world. Due to the rapid urban and industrial development of the Pearl River Delta, Hong Kong has experienced serious environmental deterioration, and more recently, food safety problems. Man-made chemicals, especially those classified as persistent organic pollutants (POPs), such as organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs) and polybrominated diphenyl ethers (PBDEs) have been major environmental issues in the Pearl River Delta region[2,3]. DDT has a wide application in agriculture and vector control. Many countries have banned the use of DDT since 1970s[1], but it continues to be used in some countries, e.g. China. China has been a major producer and consumer of DDTs in the past as it is a large agricultural country. PCBs have been used as coolants and lubricants in transformers, capacitors, and other electrical equipment due to their nonflammable and insulating properties. PBDEs are used as flame-retardant additives in plastics, electrical appliances, television sets, computer circuit boards and casing[2]. PAHs are often formed during incomplete combustion of coal, oil, gas tobacco and grilled meat. These chemicals are highly toxic, persistent, bioaccumulative and lipophilic. If they enter our food chains, they can be biomagnified and result in extremely high concentrations in higher trophic organisms, including humans. Humans can only transform and eliminate a small amount of POPs, with most of it being stored in adipose tissues[4]. Uterine leiomyoma (benign tumor) is a common disease among women, and it seems clear that it has a close relationship with estrogen levels of patients[5]. Some persistent organic pollutants have been reported to have an estrogen-like effect, attacking hormones and the endocrine system by mimicking estrogen or by disrupting cell proliferation pathways, leading to hormone interference and malfunction of reproduction organs[6]. With the above background, this research work was designed to study (1) the concentrations of POPs in adipose tissues of women with uterine leiomyoma compared with healthy females, (2) the association of POPs in subcutaneous fat and visceral fat of the patients, and (3) the correlations between their body loadings of POPs with their seafood diet, body weight-Body Mass Index (BMI) and age.

## Materials and methods

Female adipose tissue samples of ethnic Chinese residents living in Hong Kong were collected for this study. In total, there were 68 samples of which 48 samples were from 24 patients with uterine leiomyoma (i.e. each of these patients provided two types of adipose tissues - subcutaneous fat and visceral fat), and 20 samples were from the healthy control group who provided subcutaneous fat only through liposuction. The mean age of the women was 38.7 ± 7.6 years old (range: 28 to 54 years old). A detailed questionnaire was administered to each participant in relation to individual age, body weight, height, health status, birth outcomes, lifestyle and disease history. Adipose tissues were immediately frozen (-20ºC) and then freeze-dried. Then gel permeation chromatography was used to remove residual fat content in the extract and clean-up was carried out by micro-florisil column before gas chromatography – mass spectrometer (GC-MS) analysis. The recoveries of PAHs ranged from 85 to 89%, PCBs ranged from 93 to 97%, HCHs and DDTs were all over 90%, and PBDEs ranged from 70 to 120% for solvent-spiked samples.

**Results and Discussion**

Figure 1 shows the mean concentrations of OCPs, PAHs, PCBs and PBDEs in subcutaneous fat of patients with uterine leiomyoma and healthy females. The results indicated that the patient group had significantly higher contamination of HCHs (patients: 286.1; healthy control: 106.9, $p<0.01$), DDTs (1968; 1235, $p<0.01$), PCBs (191.2; 126.2, $p<0.05$), PAHs (1835; 876.0, $p<0.01$) and PBDEs (13.1; 5.36, $p<0.01$) than that in the healthy control. Because uterine leiomyoma had a close relationship with estrogen levels in female bodies[6], and these POPs had estrogen-like effects, this suggested that the chemicals can play an important role in interfering with hormone levels and the endocrine system by mimicking estrogen or by disturbing metabolism of cells. A few previous studies have also reported that DDTs, PCBs, PAHs and PBDEs in patients with uterine leiomyoma may be involved in the pathology process of this kind of disease[7,8,9].

Figure 2 shows the association of PCBs, HCHs, DDTs, PAHs and PBDEs concentrations in patients' subcutaneous fat and visceral fat. Visceral fat had higher concentrations (but not significantly higher) of all POPs studied than that in subcutaneous fat. Visceral fat was a type of fat found in the abdomen, surrounding the vital organs which was metabolized by the liver, and turned into cholesterol which can circulate in the blood [4]. This may indicate that visceral fat was metabolically more active and vascularized which may facilitate the metabolism and detoxification of POPs[10]. Therefore, it can be concluded that visceral fat could be used as an indicator to monitor a person's exposure to environmental chemicals.

Table 1 shows the correlations of body mass index (BMI), frequency of seafood consumption, age of female and concentrations of PCBs, DDTs, PAHs and PBDEs in female subcutaneous and visceral adipose tissues. With increasing BMI, there was an increasing trend in the concentrations of PCBs in subcutaneous and visceral adipose tissues. Moreover, data from concentrations of PCBs in subcutaneous adipose tissues reflected a significant linkage between BMI and PCBs levels ($p<0.05$). Similar findings were also found in a study[11] that reported that PCBs and organochlorine levels had significant correlations ($p<0.05$) with BMI. Our study indicated that BMI may be a factor influencing the body loadings of pollutants, and increased fat mass could lead to negative biological consequence. As for the seafood diet factor, there was a significant increasing trend for PCBs and DDTs ($p<0.05$) in subcutaneous adipose tissues with the frequency of seafood consumption per week. However, due to the limited sample numbers, only PCBs showed a significant increasing trend ($p<0.05$) in visceral adipose tissues. No significant differences ($p>0.05$) were observed for concentrations of PAHs and PBDEs among different groups in both subcutaneous and visceral adipose tissues. The results of PCBs in both subcutaneous and visceral adipose tissues and DDTs in subcutaneous adipose tissues were similar to our previous study concerning the correlation of DDTs and PCBs ($p<0.001$) concentrations in human milk collected in Hong Kong and seafood consumption[12]. There was an increasing trend between age and concentrations of

PCBs and DDTs in both subcutaneous and visceral adipose tissues. Concentrations of PCBs in subcutaneous adipose tissues indicated a significant correlation ($p<0.05$) with female age. In visceral adipose tissues, a significantly lower level of DDTs ($p<0.05$) was observed in the <30 age group. Similar findings were found in a study of PCBs and DDTs ($p<0.05$) in Belgian human adipose tissue and donors' age[13] and also in our previous study on PCBs and DDTs ($p<0.001$) levels in adipose tissue of human milk and donors' age in Hong Kong[12]. The results indicated that these pollutants were persistent in the environment and did not degrade easily, and exerted harmful effects on human health through long-term exposure and accumulation.

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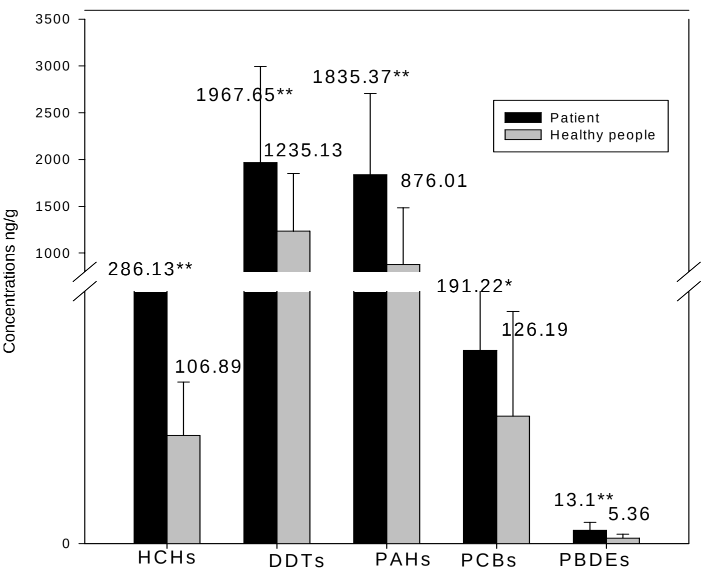


*p<0.05, **p<0.01 between patients and healthy control (Student t-test)

Figure 1.

POPs concentrations in adipose tissue between patients and healthy people

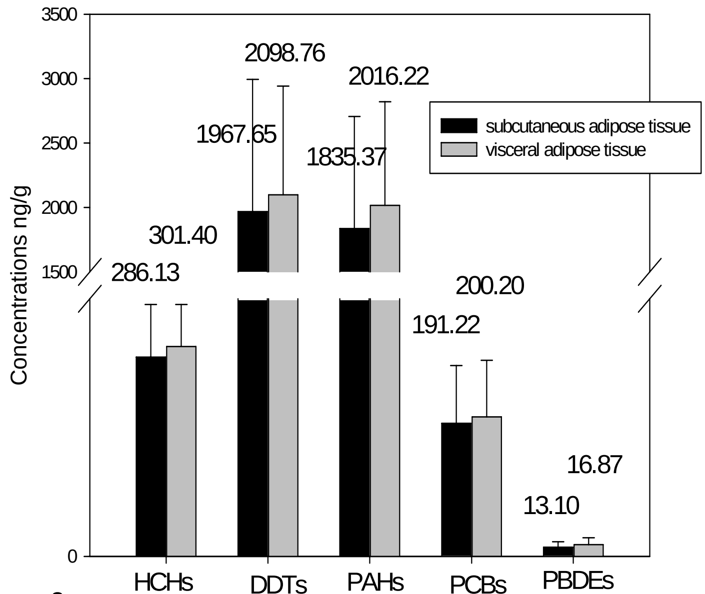


Figure 2.

POPs concentrations in subcutaneous and visceral adipose tissues of patients

**Table 1**. Correlations between POPs concentrations (ng/g fat) and BMI, seafood consumption and age

| Influence Factors | | No. | PCBs | DDTs | PAHs | PBDEs |
|---|---|---|---|---|---|---|
| BMI | *Subcutaneous adipose tissue* | | | | | |
| | <18 | 4 | 134±72.6a | 1459±899a | 1173±710a | 7.64±3.95a |
| | 19-20 | 14 | 159±71.5a | 1711±813a | 1929±795a | 12.1±10.8a |
| | 21-22 | 7 | 150±105a | 2269±1509a | 1188±409a | 13.0±6.76a |
| | 23-24 | 7 | 216±83.5ab | 1397±565a | 1395±735a | 10.9±4.89a |
| | >25 | 3 | 257±204b | 847±150a | 2079±2005a | 8.51±3.58a |
| | *Visceral adipose tissue* | | | | | |
| | <18 | 2 | 149±47.0a | 2478±279a | 2034±1016ab | 13.0±0.98a |
| | 19-20 | 9 | 182±74.2a | 1877±906a | 2238±715ab | 19.7±14.8a |
| | 21-22 | 6 | 244±67.3a | 2408±1086a | 1680±635ab | 16.1±7.03a |
| | 23-24 | 4 | 206±139a | 1900±735a | 1057±60.2a | 13.5±5.01a |
| | >25 | 3 | 217±7.50a | 2386±596a | 2964±712b | 20.0±2.38a |
| Seafood consumption (times/week) | *Subcutaneous adipose tissue* | | | | | |
| | <3 | 13 | 113±64.0a | 980±391a | 1489±968a | 8.45±5.06a |
| | 4-6 | 9 | 119±47.6a | 1390±578ab | 1507±857a | 14.8±13.2a |
| | 7-8 | 6 | 148±33.5ab | 1517±517ab | 977±322a | 10.3±4.71a |
| | >9 | 10 | 223±55.3b | 2221±528b | 1901±725a | 10.4±1.66a |
| | *Visceral adipose tissue* | | | | | |
| | <3 | 6 | 160±81.0a | 2101±1355a | 1784±1040a | 14.2±3.27a |
| | 4-6 | 5 | 182±107a | 1557±823a | 2481±516a | 26.9±18.9b |
| | 7-8 | 5 | 210±98.5ab | 2183±269a | 1445±556a | 15.4±5.24a |
| | >9 | 8 | 229±45.9b | 2444±476a | 2244±625a | 13.5±2.42a |
| Age | *Subcutaneous adipose tissue* | | | | | |
| | <30 | 8 | 97.7±43.3a | 1019±484a | 1241±634a | 4.98±2.92a |
| | 31-35 | 10 | 124±47.7a | 1334±704a | 1960±1013a | 12.8±12.2a |
| | 36-39 | 6 | 192±119ab | 1776±805a | 1568±1364a | 12.6±8.99a |
| | 40-46 | 13 | 161±76.6ab | 1984±575a | 1090±561a | 9.18±3.27a |
| | >47 | 7 | 248±144b | 2002±1291a | 1032±836a | 9.85±4.81a |
| | *Visceral adipose tissue* | | | | | |
| | <30 | 2 | 150±87.1a | 702±15.0a | 1758±1407a | 16.3±3.73a |
| | 31-35 | 4 | 162±27.7a | 1930±628b | 2434±1076a | 23.7±21.5a |
| | 36-39 | 4 | 179±70.1a | 2388±514b | 2379±214a | 22.9±7.56a |
| | 40-46 | 10 | 243±100ab | 2313±1004b | 1737±282a | 12.9±4.03a |
| | >47 | 4 | 273±89.5b | 2293±630b | 1826±895a | 14.4±3.90a |

Values are presented in mean ± standard deviation, with n=3. Values followed by the same letter on the same column are not significantly different at the 0.05 probability level according to Duncan's Multiple Range Test