EnvironmentAsia
The international journal published by the Thai Society of Higher Education Institutes on Environment

Available online at www.tshe.org/EA
EnvironmentAsia 7(2) (2014) 1-6

Bioaccumulation of DDT Residues in Human Serum: an Historical Use of DDT Indoor Residual Spraying in Malaria Endemic Regions of Thailand

Punthip Teeyapant, Sujitra Sikaphan and Sittiporn Parnmen

Division of Toxicology, Department of Medical Sciences, Ministry of Public Health, Nonthaburi 11000, Thailand

Abstract

In Thailand, DDT indoor residual spraying (IRS) was used to interrupt malaria transmission until it was phased out between 1995 and 1999. However, contamination by DDT and its primary metabolite, *p,p′*-DDE remains a serious environmental and human health concern. We investigated serum concentrations of *p,p′*-DDE and *p,p′*-DDT in Southern Thai residents living in malaria-endemic areas where IRS with DDT was applied. Levels of *p,p′*-DDE and *p,p′*-DDT were measured in plasma serum of 346 participants (205 females, 141 males) from Southern provinces of Thailand and from Bangkok. Serum concentrations of measured compounds were significantly higher in Southern Thai residents than general population (in Bangkok) ($P < 0.001$). The highest geometric mean value of *p,p′*-DDE was 6,531 (95% CI=4,083-8,979) and 5,053 (95% CI=2,909-7,197) ng/g lipids in female and male subjects, respectively. Even though, DDT ultimately is banned for all uses, the concentration of the daughter compound *p,p′*-DDE was much higher in Southern subjects than in the general population. A high ratio of *p,p′*-DDE/*p,p′*-DDT indicates that the exposure is due to past rather than recent use of DDT.

Keywords: Bioaccumulation; DDT ratio; indoor residual spraying; serum concentrations; Thailand

1. Introduction

The organochlorine insecticide, 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (DDT) is a persistent organic pollutants (POPs), which historically was used widely in agricultural pest control and for control of vector-borne diseases in Thailand. DDT is converted in the environment to other more stable forms, including 1,1-dichloro-2,2-bis (*p*-chlorophenyl) ethane (*p,p′*-DDD) and 1,1-dichloro-2,2-bis (*p*-chlorophenyl) ethylene (*p,p′*-DDE). Similar to the mother compound these degradation products are highly persistent in the environment, they bioaccumulate, and may undergo biomagnificantion food chains (Thomas *et al*., 2008).

In 1949, DDT was first introduced for malaria vector control as an indoor residual spray (IRS) in Thailand and was simultaneously used for agricultural pest control (Chareonviriyahpap *et al*., 2000). Malaria was a major public health problem in our country. During 1970s-1980s, IRS by DDT was a main vector control procedure for the Malaria Control Program (MCP). Since 1983, the use of DDT in agriculture was banned. Later, in 1995, the import of this chemical was stopped; however, there was still DDT stocks leftover (Chareonviriyahpap *et al*., 1999; 2000). In 1985, Malaria surveillance activities in Thailand recorded a total of malaria 275,443 cases peaking to 349,291 cases in 1988, and declining thereafter to 85,625 cases since 1995 (Chareonviriyahpap *et al*., 2000). Nevertheless, there was re-emergence of malaria transmission in various parts of the country during 1998-2000, especially in the Southern provinces (Konchom *et al*., 2005). Hence, the remaining stock of DDT was used for vector control until it was phased out between 1995 and 1999 (Chareonviriyahpap *et al*., 2000). *Plasmodium falciparum* and *P. vivax* are commonly found in the Southern regions (Chareonviriyahpap *et al*., 1999). Nowadays, malaria cases have decreased by 75%, judging from reported cases between 2000 and 2011 (World Health Organization, 2012).

In this study we investigated serum concentrations of *p,p′*-DDE and *p,p′*-DDT as a result of a past use of IRS program in Southern peninsula areas (Chumphon, Phuket, Krabi and Satun) Control studies were carried out in Bangkok. As expected, the degradation products of DDT were still increased in Thai Southern population, especially in adult subjects.

2. Materials and Methods

2.1. Subjects

The study was approved by the Ethical Review Committee for Research in Human Subjects at Department of Medical Sciences, Ministry of Public Health (Thailand). All participants signed a written informed consent form. Demographics information, health behavior, questions on diet, education and

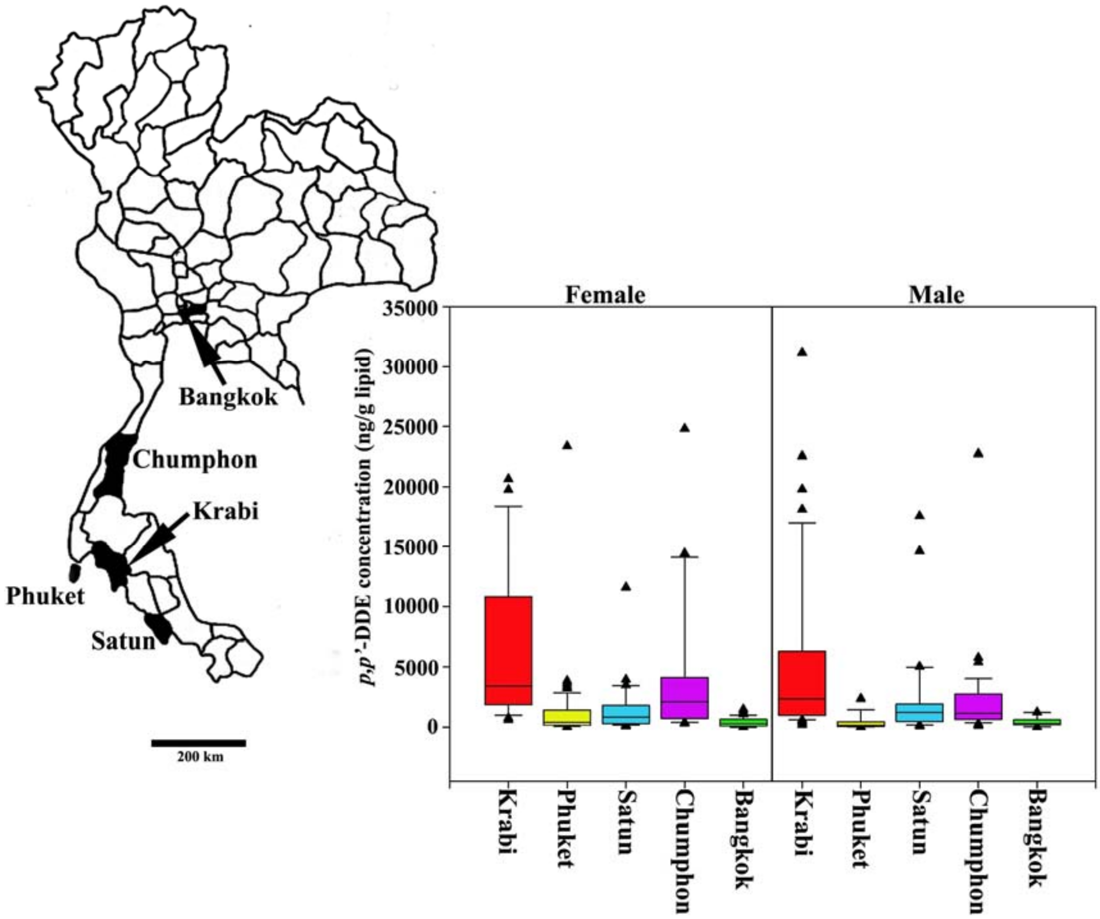

Figure 1. Box plots showing of serum *p,p′*-DDE and *p,p′*-DDT concentrations in Southern Thai population

occupation were registered. We recruited subjects in the five participating regions in Thailand (Fig. 1) during May to August 2011. A total of 346 subjects (205 females and 141 males, respectively) were examined. At enrollment, the mean age of all female participants was 46±12 years. The mean age of all male participants was 48±12 years. The control region was located in Bangkok that expected to be low background level of exposure to DDT.

2.2. Measurements in blood serum

For each subject 10 ml of blood was obtained by venipuncture between 8 and 10 a.m. after an overnight fast. The blood was allowed to clot at room temperature and was then centrifuged in a refrigerated centrifuge. The blood sample of 10 ml was collected in a Vacuette® silicone tube without an anticoagulant agent for analyses of cholesterol, *p,p′*-DDE, *p,p′*-DDT and triglycerides. The aliquots of serum were stored at -80°C until being transported to the laboratories analysis. BMI was measured weight/height^2 (kg/m^2).

Serum total cholesterol and triglycerides concentrations were determined using enzymatically methods by Professional Laboratory Management Corp. Co., Ltd (Thailand), which is accredited for those analyses.

Serum total *p,p′*-DDE and *p,p′*-DDT concentrations were measured using gas chromatography with tandem mass spectrometry (Agilent 7890 GC & Agilent 7000 Triple Quadrupole GC/MS system, USA). The standards were purchased from Chem Service (USA). Isodrin was used as internal standard. The limit of quantification (LOQ) was set to ten times the average noise for each compound. Quantification was achieved using National Institute of Standards & Technology's certified reference material (USA). None of the compounds were detected in blanks. The LOQ was determined by the lowest calibration level. Quantitative limit was 0.12 µg/l with the correlation coefficient value of *0.9995*. The coefficient of variation for the analyzed compound was less than 10%. Recovery varied from 78% to 110% for these compounds. The serum total lipids concentrations for the adjustment of *p,p′*-DDE and *p,p′*-DDT toxicant were calculated by the following formula (Phillips *et al*., 1989; Bernert *et al*., 2007): Total lipids (mg/dl) = 2.27 x total cholesterol (mg/dl) + triglycerides (mg/dl) + 62.3.

Table 1. Characteristics of the study subjects

Regions	Sex (N)	Age±SD (yr)	BMI (kg/m2)
Chumphon	Female (n=37)	45±7	23±3
	Male (n=37)	43±7	21±3
Krabi	Female (n=29)	45±12	25±4
	Male (n=41)	49±11	22±3
Phuket	Female (n=59)	43±12	25±4
	Male (n=14)	42±13	25±4
Satun	Female (n=32)	44±10	25±4
	Male (n=30)	50±14	24±8
Control site	Female (n=48)	52±10	26±5
	Male (n=19)	56±15	22±4

2.3. Data and statistical analysis

All data analyzes were performed using Sigma Plot for Windows (version 11.0, Systat Software, Chicago, IL). The values below the LOQ were treated as half of this limit. Data was presented as mean with 95% confidence interval as well as interquartile range of concentrations. Statistical comparison of *p,p´*-DDE and *p,p´*-DDT concentrations among the five regions was performed using the Kruskal-Wallis one-way ANOVA test.

3. Results

Characteristics of the study subjects are presented in Table 1. We chose to study adult subjects because they were alive longer during the period when DDT was used in Thailand. They had a greater opportunity for high background levels due to exposure to the insecticide. The serum concentrations of organochlorine compounds, expressed as ng/g lipid are summarized in Table 2. A Kruskal-Wallis one-way ANOVA test demonstrated a significant difference in serum

Table 2. Mean serum concentrations of organochlorine insecticide DDT (ng/g lipid), with 95% confidence interval in parentheses

Regions	Sex	*p,p´*-DDE	<LOQ	*p,p´*-DDT	<LOQ	*p,p´*-DDE/ *p,p´*-DDT ratio
Chumphon	Female (n=37)	3939 (2178-5700)	2	254 (142-366)	0	23 (16-29)
	Male (n=37)	2294 (1054-3533)	0	145 (95-195)	1	23 (12-33)
Krabi	Female (n=29)	6531 (4083-8979)	0	344 (214-474)	0	26 (17-34)
	Male (n=41)	5053 (2909-7197)	0	198 (97-300)	3	42 (26-58)
Phuket	Female (n=59)	1221 (416-2026)	1	80 (18-142)	35	35 (24-46)
	Male (n=14)	382 (33-730)	1	19 (2-35)	10	25 (6-44)
Satun	Female (n=32)	1504 (732-2277)	4	84 (46-121)	0	22 (16-27)
	Male (n=30)	2365 (888-3842)	0	113 (16-210)	4	29 (21-38)
Bangkok Control site	Female (n=48)	431 (320-542)	6	20 (16-23)	43	24 (17-31)
	Male (n=19)	407 (229-585)	0	18 (13-27)	18	24 (13-34)

LOQ are the number of subjects below the limit of quantification that were substituted with half of this limit

Table 3. Median serum concentrations of organochlorine insecticide DDT (ng/g lipid), with interquartile ranges (IQR) in parentheses

Sex	Regions (n)	*p,p′*-DDE	Kruskal-Wallis H (P-value)	*p,p′*-DDT	Kruskal-Wallis H (*P*-value)
Female	Chumphon (n=37)	2092 (752-3921)	H=79.414 *P*<0.001	104 (48-341)	H=92.512 *P*<0.001
	Krabi (n=29)	3410 (906-9340)		247 (64-485)	
	Phuket (n=59)	399 (168-1410)		11 (9-27)	
	Satun (n=32)	836 (308-1781)		32 (22-107)	
	Control site (n=48)	288 (122-644)		17 (14-19)	
Male	Chumphon (n=37)	1139 (662-2720)	H=52.224 *P*<0.001	78 (46-204)	H=56.854 *P*<0.001
	Krabi (n=41)	2343 (999-6198)		64 (42-188)	
	Phuket (n=14)	152 (70-441)		10 (9-15)	
	Satun (n=30)	1223 (492-1704)		39 (22-83)	
	Control site (n=19)	285 (201-598)		18 (15-19)	

p,p′-DDE and *p,p′*-DDT concentrations between regions (Table 3). All subjects living in Southern peninsular regions had higher levels of *p,p′*-DDE as compared to subjects from control site (Fig. 1; Table 2). The highest geometric mean concentration of *p,p′*-DDE was observed in the Krabi province (female: 6,531 (95% CI=4,083-8,979) and male: 5,053(95% CI=2,909-7,197) ng/g lipids, respectively). The second-highest concentrations of *p,p′*-DDE were found in Chumphon province (female: 3,939 (95% CI=2,178-5,700) and males: 2,294 (95% CI=1,054-3,533) ng/g lipids, respectively). Similarly, levels of *p,p′*-DDT was found to be highest in both provinces (Table 2). The lowest serum concentrations of *p,p′*-DDE and *p,p′*-DDT were found in the control site, most of the values were below the LOQ (Table 2). Furthermore, the *p,p′*-DDE/*p,p′*-DDT ratios ranged from 6 to 58 (Table 2).

4. Discussion

In Thailand, DDT insecticide has been used in both agricultural practices and public health purposes such as the malaria control program (Chareonviriyahpap *et al*., 1999; 2000). DDT indoor residual spraying was first used in the northern Thailand in 1949s and has been decreasing overtime for malaria control use. However, an outbreak in 1986 in the southern provinces resulted in a rise to more than 350,000 cases by 1987 (Konchom *et al*., 2005). Another outbreak throughout the southern provinces, again, generated 131,000 cases from 1998 to 2000 (Konchom *et al*., 2005). So, IRS with DDT was still used in vector control until it was completely withdrawn in 2001. The main reason for the withdrawal of DDT from the MCP because of insecticide resistance was observed in mosquito vectors, and its impact on the environment (Chareonviriyahpap *et al*., 1999). In 2001, all of the organochlorine insecticides classified under the Stockholm Convention as persistent organic pollutants (POPs) were prohibited or banned from use, import, export and production in the country (Pollution Control Department, 2013).

The high lipid solubility of DDT enables it to accumulate in the lipophilic component of the plasma in the body (Jaga and Dharmani, 2003). The half-life of this insecticide in serum is approximately 10 years (Turusov *et al*., 2002). Several studies have reported the insidious effects of DDT on humans and animals (Alava *et al*., 2011; Asawasinsopon *et al*., 2006; Chevrier *et al*., 2008). Some epidemiologic studies have shown that *p,p′*-DDE exposure may be a risk factor for obesity, dyslipidemia, insulin resistance and common precursors of type II diabetes, as well as cardiovascular disease (Lee *et al*., 2011; Rignell-Hydbom *et al*., 2009).

For these reasons, we chose to study local Thai people who resided in the areas where the IRS program was applied. We found high concentrations with wide variation of the compounds *p,p´*-DDE and *p,p´*-DDT in serum of both male and female subjects living in Southern peninsular areas where the prevalence of malaria was high and IRS program was applied. The highest *p,p´*-DDE and *p,p´*-DDT concentrations were found in Krabi and Chumphon provinces. However, the concentrations of *p,p´*-DDT are on average over 15 times lower than the concentration of *p,p´*-DDE. Previous articles have reported concentration of *p,p´*-DDE in maternal serum from Northern Thailand where ISR with DDT was first used (Asawasinsopon *et al*., 2006). The reported serum concentration of *p,p´*-DDE was 1,191 ng/g lipid (Asawasinsopon *et al*., 2006).

The median serum concentrations of *p,p´*-DDE and *p,p´*-DDT in the present study are low compared to the concentrations of the same compounds in serum from other countries with endemic malaria regions, such as regions in South Africa (median 4,092 and 2,788 ng/g lipids, respectively) (Channa *et al*., 2012), China (median 7,635 and 309 ng/g lipids, respectively) (Lee *et al*., 2007), and Bangladesh (median 2,900-3,900 and 370-670 ng/g lipids, respectively) (Mamum *et al*., 2007).

The changes in ratio of *p,p´*-DDE/ *p,p´*-DDT is an indicator of whether the DDT was recently released or had been emitted to the environment (Hauser *et al*., 2003; Delport *et al*., 2011). A relatively low *p,p´*-DDE/*p,p´*-DDT ratio and a high concentration of *p,p´*-DDT are indicative of more recent exposures to DDT. Conversely, relatively high ratios and low concentrations of *p,p´*-DDT imply a past usage of DDT. In this study, we found on an average high ratios with low concentration of *p,p´*-DDT in serum of Southern Thai residents, indicating that the DDT exposure was recent.

5. Conclusions

Our results show that organochlorine insecticide DDTs are detectable in the serum despite their ban a few decades ago. The high bioaccumulation of *p,p´*-DDE in Southern Thai residents could be explained by an historical use of DDT in the malaria control program. This information should be regarded an early warning of pollution threat to human health and environment. Further research should continuously monitor DDT residues in order to better understand the relationship between DDT and disease risk.

Acknowledgements

The authors confirm that there are no potential conflicts of interest involved in this study. The Department of Medical Sciences (Ministry of Public Health: Thailand) financially supported this work.

References

Alava JJ, Ross PS, Ikonomou MG, Cruz M, Jimenez-Uzcátegui G, Dubetz C, Salazar S, Costa DP, Villegas-Amtmann S, Howorth P, Gobas FAPC. DDT in endangered Galapagos sea lions (*Zalophus wollebaeki*). Marine Pollution Bulletin 2011; 62: 660-71.

Asawasinsopon R, Prapamontol T, Prakobvitayakit O, Vaneesorn Y, Mangklabruks A, Hock B. The association between organochlorine and thyroid hormone levels in cord serum: a study from northern Thailand. Environment International 2006; 32(4): 554-59.

Bernert JT, Turner WE, Patterson DGJr, Needham LL. Calculation of serum "total lipid" concentrations for the adjustment of persistent organohalogen toxicant measurements in human samples. Chemosphere 2007; 68(5): 824-31.

Channa K, Röllin HB, Nøst TH, Odland JØ, Sandanger TM. Prenatal exposure to DDT in malaria endemic region following indoor residual spraying and in non malaria coastal region of South Africa. Science of the Total Environment 2012; 429: 183-90.

Chareonviriyahpap T, Aum-aung B, Ratanatham S. Current insecticide resistance patterns in mosquito vectors in Thailand. The Southeast Asian Journal of Tropical Medicine and Public Health 1999; 30(1): 184-94.

Chareonviriyahpap T, Bangs MJ, Ratanatham S. Status of Malaria in Thailand. The Southeast Asian Journal of Tropical Medicine and Public Health 2000; 31(2): 225-37.

Chevrier J, Eskenazi B, Holland N, Bradman A, Barr DB. Effects of exposure to polychlorinated biphenyls and organochlorine pesticides on thyroid function during pregnancy. American Journal of Epidemiology 2008; 168(3): 298-310.

Delport R, Bornman R, Maclntyre UE, Oosthuizen NM, Becker PJ, Aneck-Hahn NH, de Jager C. Changes in retinol-binding protein concentrations and thyroid homeostasis with nonoccupational exposure to DDT. Environmental Health Perspective 2011; 119(5): 647-51.

Hauser R, Chen Z, Pothier L, Ryan L, Altshul L. The relationship between human semen parameters and environmental exposure to polychlorinated biphenyls and *p,p´*-DDE. Environmental Health Perspective 2003; 111(12): 1505-11.

Jaga K, Dharmani C. Global surveillance of DDT and DDE levels in human tissues. International Journal of Occupational Medicine and Environmental health 2003; 16(1): 7-20.

Konchom S, Singhasivanon P, Kaewkungwal J, Chuprapawan S, Thimasarn K, Kidson C, Yimsamran S, Rojanawatsirivet C. Chronicle of malaria epidemics in Thailand, 1980-2000. The Southeast Asian Journal of Tropical Medicine and Public Health 2005; 36: 64-67.

Lee SA, Dai Q, Zheng W, Gao YT, Blair A, Tessari JD, Tian JiB, Shu XO. Association of serum concentration of organochlorine pesticides with dietary intake and other lifestyle factors among urban Chinese women. Environment International 2007; 33(2): 157-63.

Lee DH, Steffes MW, Sjödin A, Jones RS, Needham LL, Jacobs DR Jr. Low dose organochlorine pesticides and polychlorinated biphenyls predict obesity, dyslipidemia, and insulin resistance among people free of diabetes. PLoS ONE 2011; 6(1): 1-9.

Mamum MIR, Zamir R, Nahar N, Mosihuzzaman M, Linderhilm L, Athanasiadou M, Bergman A. Traditional organochlorine pollutants in blood from humans living in the Bangladesh capital area. Organohalogen Compounds 2007; 69: 2026-30.

Phillips DL, Pirkle JL, Burse VW, Bernert JTJr, Henderson LO, Needham LL. Chlorinated hydrocarbon levels in human serum: effects of fasting and feeding. Archives of Environmental Contamination and Toxicology 1989; 18(4): 495-500.

Pollution Control Department. Stockholm convention on persistent organic pollutant (POPs), as amended in 2011. BTS press, Bangkok, Thailand. 2013.

Rignell-Hydbom A, Lidfeldt J, Kivirant H, Rantakokko P, Samsioe G, Agardh C-D, Rylander L. Exposure to *p,p′*-DDE: a risk factor for type 2 diabetes. PLoS ONE 2009; 4(10): 1-6.

Thomas JE, Ou LT, Al-Agely A. DDE remediation and degradation. Reviews of Environmental Contamination and Toxicology 2008; 194: 55-69.

Turusov V, Rakitsky V, Toamtis L. Dichlorodiphenyltrichloroethane (DDT): ubiquity, persistence, and risks. Environmental Health Perspective 2002; 110(2): 125-28.

World Health Organization. World Malaria Report 2012. Geneva: World Health Organization; 2011.

Received 26 March 2014
Accepted 18 April 2014

Correspondence to
Dr.Sittiporn Parnmen
Division of Toxicology,
Department of Medical Sciences,
Ministry of Public Health,
Nonthaburi 11000,
Thailand
E-mail: sittiporn.p@dmsc.mail.go.th