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EFFECT OF ORGANOCHLORINES ON HUMAN ENDOCRINE SYSTEM
ผลของสารออร์กาโนคลอรีนต่อระบบต่อมไร้ท่อของมนุษย์

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Abstract

Organochlorines are classified as persistent organic pollutants and endocrine disrupters. They were widely used for insect control and malaria vector control programs. Although most organochlorines were officially banned in many countries, high levels have been found in ecosystem and food chain. Because organochlorines act as endocrine disrupters and lipid soluble chemicals, it is difficult to excrete these environmental pollutants from the body, and consequently caused adverse effects on endocrine system in wildlife and humans. Epidemiological studies have suggested that exposure to organochlorines in adults linked with an increase incidence of reproductive tract abnormalities, decreased sperm quantities and qualities, and reproductive cancers. Furthermore, prenatal and postnatal exposure to organochlorines have been suggested to link with an increase risk of preterm birth, low birth weight, birth defect, acute infection, cryptorchidism, and hypospadia. Many scientists have concerned that low level of prenatal organochlorine exposure may cause irreversible changes during development and affect later functioning in adult life, and they would be warrant further detail investigations.

Keywords: organochlorines, persistent organic pollutants, endocrine disrupters, xenoestrogens, DDT, pesticides

บทคัดย่อ

สารออร์กาโนคลอรีนเป็นสารเคมีที่จัดอยู่ในกลุ่มสารมลพิษที่ตกค้างยาวนาน และเป็นสารเคมีที่ก่อกวนระบบต่อมไร้ท่อ ในอดีต สารเคมีกลุ่มนี้นิยมใช้กันอย่างแพร่หลายในการควบคุมแมลงทางเกษตรกรรม และใช้ในการควบคุมยุงก้นปล่องที่เป็นพาหะของโรคมาลาเรีย ถึงแม้ว่าปัจจุบันสารออร์กาโนคลอรีนจะถูกประกาศห้ามใช้อย่างเป็นทางการในหลายประเทศแล้วก็ตาม แต่ระดับการตกค้างของสารเคมีกลุ่มดังกล่าวยังคงมีปริมาณสูงในระบบนิเวศและห่วงโซ่อาหาร เนื่องจากสารออร์กาโนคลอรีนจัดเป็นสารเคมีที่ก่อกวนระบบต่อมไร้ท่อ และเป็นสารที่ละลายในไขมัน จึงยากที่จะกำจัดออกจากร่างกาย ทำให้เกิดการตกค้างและสะสมในร่างกาย

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และก่อให้เกิดผลเสียต่อระบบต่อมไร้ท่อของสัตว์และมนุษย์ตามมา จากการศึกษาทางวิทยาการระบาดพบว่า การสัมผัสสารออร์กาโนคลอรีนในวัยเจริญพันธุ์มีความสัมพันธ์กับการเพิ่มขึ้นของอัตราอุบัติการณ์ของความผิดปกติของโรคระบบสืบพันธุ์ และโรคมะเร็งระบบสืบพันธุ์ รวมถึงปริมาณและคุณภาพของอสุจิลดลง การสัมผัสสารออร์กาโนคลอรีนของทารกแรกเกิดตั้งแต่อยู่ในครรภ์มารดาผ่านทางสายสะดือ และการสัมผัสสารออร์กาโนคลอรีนจากการรับประทานนมมารดามีความสัมพันธ์กับการคลอดก่อนกำหนด น้ำหนักแรกเกิดน้อย ลูกวิรูป การติดเชื้อเฉียบพลัน และอวัยวะเพศผิดปกติ ซึ่งผลการวิจัยจำนวนมากทำให้ตระหนักถึงเรื่องการสัมผัสสารออร์กาโนคลอรีนในทารกขณะอยู่ในครรภ์มารดาอาจส่งผลกระทบต่อการพัฒนาของทารกและต่อการทำหน้าที่ของอวัยวะในร่างกายอย่างถาวร ซึ่งจะต้องทำการศึกษาวิจัยต่อไปในอนาคต

คำสำคัญ: ออร์กาโนคลอรีน มลพิษอินทรีย์ตกค้างยาวนาน สารก่อกวนต่อมไร้ท่อ ดีดีที ซีโนเอสโตรเจน สารเคมีปราบศัตรูพืช

Introduction

Organochlorines are chemicals that are toxic, persist in the environments for long periods, bio-accumulate through food chain, and pose a risk of causing harmful effects on wildlife and humans. They include aldrin, chlordane, dichlorodiphenyl-trichloroethane (DDT), dieldrin, endrin, heptachlor, hexachlorobenzene (HCB), mirex and toxaphene. DDT and their metabolites are the major compounds found in the environment, wildlife, and humans[1-6].

Organochlorines were widely used for insect control and malaria vector control programs. Uses of organochlorines, and DDT in particular, enormously increased after the Second World War because of their effectiveness against mosquitoes and other insects. However, problem related to extensive use of DDT began to appear in the year after the 1940s. Consequently, DDT has been banned since the 1970s in most developed countries although it is still used in some developing countries for essential public health purposes[4]. In Thailand, using DDT for agricultural purposes has been banned since 1983; however, its use for public health was completely banned in 1999[7-8]. Although most organochlorines were officially banned in Thailand, high levels have been found in environment and humans[9-13]. The banned years of individual organochlorines in Thailand are presented in Table 1[14]. The current intakes of organochlorines in Asia are up to 100 times greater than those in developed countries, and the estimated intake of DDT by children is reported to be 100 times greater than the acceptable daily intake (ADI) established by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO)[4].

Table 1 The banned years of individual organochlorines in Thailand

Organochlorines	The banned year
aldrin	1988
chlordane	2000
DDT	1983 (Farming purposes)
	1999 (malaria control programs)
dieldrin	1988
HCB	1980
Heptachlor	1988
Toxaphene	1983

Source: Department of Agriculture, 2002[14].

Organochlorines act as endocrine disrupters

A number of the reports have indicated that organochlorines act as endocrine disrupting chemicals. These chemicals can exert their effects in many ways including[15-17]:

(1) mimicking the effects of natural hormones (like estrogens and androgens) by binding to the hormone receptor.

(2) antaginising the effects of natural hormones by blocking the binding to the hormone receptor.

(3) reacting with the natural hormone structure to alter its structure.

(4) interfering to natural hormone synthesis.

(5) interfering to the transport and elimination of natural hormones.

Toxicokinetics

Organochlorines can be found in every level of food chain. Humans are placed at the top of food chain, therefore high levels of organochlorines have been found in the human body[3, 18, 19]. Exposure to organochlorines can occur through the direct contact with pesticides and through the ingestion of contaminated water, food, or air. Once inside the body, these contaminants can be readily stored in fatty tissue where they cannot exert any effects. However, when fat is mobilized for energy, these chemicals are consequently released into bloodstream and cause adverse health effects. Because of their lipophilic property, it is difficult to excrete from the body[20]. However, pregnant women can excrete these compounds in milk during breast-feeding. Organochlorines and their

metabolites are released from fatty tissue into the bloodstream during pregnancy and breastfeeding and subsequently transferred to their offsprings[13, 21]. Since fetuses and infants may not have adequate defense mechanisms to protect themselves from exposure to toxicants, they therefore become a vulnerable group[22-23].

Endocrine disrupting effects of organochlorines

(1) Effects on adults:

Studies in field and laboratory animals have found that exposure to organochlorines was linked to abnormal hormonal status, reduced fertility, undescended testicle, altered sexual behavior, and feminization of male[1, 24-27]. Human epidemiological studies have concerned with the association between exposure to these contaminants and endpoints of adverse health outcomes. The potential human effects of individual organochlorines are presented in Table 2[28].

A number of the studies have found that exposure to organochlorines linked to an increased incidence of reproductive tract abnormalities (hypospadia and cryptorchidism), decreased sperm quantities and qualities, and testicular and prostate cancers in men.[29-37] It has also linked to an increased incidence of early puberty, impaired lactation, and breast cancer in women[34, 36, 38-41]. However, few recent studies investigated their effects on hormonal status in humans and available data are inconclusive.

Table 3 presents DDT levels and their association with reproductive hormones in men from different countries. DDT in North Carolina farmers, Latvian and Swedish men, and Italian men found no effect on reproductive hormonal status[42-44]. On the other hand, the studies in Mexican men and South African male workers found an effect on hormonal status. The study in Mexican men found a negative association of plasma *p,p′*-DDE levels with the ratio of bio-available to total testosterone, semen volumes, and sperm counts(30). The study in South African male workers found positive associations of *p,p′*-DDT and *p,p′*-DDD with estradiol (E2) and testosterone; however, they suggested that these associations might be due to chance, since *p,p′*-DDT and *p,p′*-DDD were not known to be a strongly anti-androgenic or estrogenic[45-46]. The study in Thai male farmers found negative associations of *p,p′*-DDE and *p,p′*-DDT with E_2. However, these associations were rather weak. It might be due to low levels of DDT exposure as a factor limiting interpretation[10].

Table 2 Potential human effects of individual organochlorines

Health Effects	Aldrin, Dieldrin	Chlordane	DDT	Toxaphene	Mirex	HCH
Reproduction and development	+	+	+	+	+	+
Cytochrome P450 system	+	+		+	+	+
Porphyria						+
Immune system	+	+	+	+	+	+
Adrenal effects			+	+		+
Thyroid and retinal effects			+	+		+
Mutagenic effects						
Carcinogenic effects	+	+		+	+	+
Skeletal changes				+		

Source: Papiya, 2004[28].

Table 3 Mean or median levels of DDT and its metabolites expressed on a lipid basis and their association with reproductive hormone in men from different countries

Authors	Study population	Mean or median of DDT-related compounds, ng/g lipids		Association
		p,p′-DDE	p,p′-DDT	
Ayotte et al. (2001)[30]	Mexican men (n=24)	77,900	n/r [b]	Decreased testosterone
Dalvie et al. (2004a,b)[45-46]	South african workers (n=47)	65,000	26,100	Increased E2 and testosterone
Asawasinsopon et al. (2006)[10]	Thai adult men (n=97)	4,013	628.7	Decreased E2
Martin, Jr. et al. (2002)[43]	North Carolina farmers (n=137)	1,213[a]	n/r[b]	No association
Hagmar et al. (2001)[42]	Latvian and Swedish men (n=110)	828	50	No association
Cocco et al. (2004)[44]	Italian men (n=107)	396	47	No association

[a] Mean level of DDE, b n/r = not reported

Source: Asawasinsopon et al., 2006[10]

(2) Effects on pregnant women and infants:

Organochlorines have an ability to be transfered from mothers to infant through placenta barrier and breastmilk[11, 13, 47-51]. Studies have mentioned that exposure during fetus and infant development may result in a permanent change of immune system, endocrine system, and neurodevelopment in infants even at low levels of exposure[50, 52-54]. Epidemiological studies have related prenatal and postnatal exposure to these contaminants with an increased risk of preterm birth, low birth weight, birth defect, acute infection, cryptorchidism, hypospadia, and congenital hypothyroidism[54-62].

The effects of organochlorines on thyroid hormone status have been reviewed. The study of Asawasinsopon et al. (2006)[11] found a negative association of cord serum *p,p′*-DDE, *p,p′*-DDT, and *o,p′*-DDE levels with cord serum total thyroxine (TT_4) levels. However, TT_4 levels of most infant subjects (92.3%) were within the normal range. It is possible that serum DDT levels might not be high enough to have an obvious effect on hormonal metabolism. The study of Alvarez-Pedrerol et al. (2008)[63-64] found a negative association of blood levels of p,p'-DDT, beta-HCH with total Triiodothyronine (TT3) levels in preschool children. Thyroid hormones play an important role in brain and neurodevelopment of infants. Therefore, the small change of thyroid hormone levels may cause irreversible changes during development and affect later functioning in adult life.

Conclusions

Although organochlorines have been banned for long periods, they are still found in ecosystem and food chain. Humans are placed at the top of food chain, therefore high levels of organochlorines have been found in the human body. A number of studies have indicated that organochlorines act as endocrine disrupter; therefore, they also cause harmful health effects to endocrine system in humans. Epidemiological studies have suggested that:

(1) Exposure to organochlorines in adults linked to an increase incidenced of reproductive tract abnormalities, decreased sperm quantities and qualities, early puberty, impaired lactation, and reproductive cancers.

(2) Prenatal and postnatal exposure to organochlorines linked to an increased risk of preterm birth, low birth weight, birth defect, acute infection, cryptorchidism, hypospadia, and congenital hypothyroidism. The exposure to organochlorines also linked to changes of thyroid hormone levels in infants, and they would be warrant further detail investigations.

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